```
=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 08:41:09 ON 25 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 25 May 2004  VOL 140 ISS 22
FILE LAST UPDATED: 24 May 2004  (20040524/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d l14 bib abs hitrn retable tot

L14  ANSWER 1 OF 24  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:392483  HCAPLUS
TI   Crystals of insulin analogs and method for the production
     thereof
IN   Berchtold, Harald
PA   Aventis Pharma Deutschland GmbH, Germany
SO   PCT Int. Appl., 28 pp.
     CODEN: PIXXD2
DT   Patent
LA   German
FAN.CNT 1
     PATENT NO.         KIND  DATE          APPLICATION NO.  DATE
     ---------------    ----  --------      ---------------  --------
PI   WO 2004039838      A1    20040513      WO 2003-EP11470  20031016
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG,
             KZ, MD, RU, TJ
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
             CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC,
             NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
             GW, ML, MR, NE, SN, TD, TG
     DE 10250297         A1    20040519      DE 2002-10250297 20021029
PRAI DE 2002-10250297    A     20021029
AB   The invention relates to crystals of an insulin analog, in which
     asparagine (Asn) in position B3 of the B chain is replaced by a naturally
     occurring basic amino acid residue, and at least one amino acid residue in
     positions B27, B28 or B29 of the B chain is replaced by another
     naturally occurring neutral or acid amino acid residue. According to the
     invention, phenylalanine (Phe) can optionally be absent in position B1 of
     the B chain, and the crystals exist in space group R3 (Nr. 146) with cell
     axes A = 81.5 A ± 1 A and C = 33.3 A ± 1 A. The invention also
     relates to the production and use of said crystals, and to a pharmaceutical
     composition containing these crystals.
```

IT INDEXING IN PROGRESS
IT **9004-10-8DP**, **Insulin**, analogs
RL: BPN (Biosynthetic preparation); PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(production of crystals of **insulin** analogs)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Aventis Pharma Gmbh	2002			WO 02076495 A	HCAPLUS
Havelund, S	1998			WO 9842749 A	HCAPLUS
Hoechst Marion Roussel	1998			EP 0885961 A	HCAPLUS
Lilly Co Eli	1996			EP 0709395 A	HCAPLUS

L14 ANSWER 2 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:205620 HCAPLUS
DN 133:43782
TI Semisynthetic preparation of human **insulin** analogs containing N-methylated B24-B25 or B25-**B26** peptide bonds
AU Klasova, Lenka; Huml, Karel; Barthova, Jana; Ubik, Karel; Kasicka, Vaclav; Skarda, Josef; Hauzerova, Linda; Barth, Tomislav; Wollmer, Axel; **Brandenburg, Dietrich**; Jezek, Jan; Velek, Jiri
CS Department of Biochemistry, Charles University, Prague, 128 40, Czech Rep.
SO Collection Symposium Series (1999), 3(Biologically Active Peptides), 85-87
CODEN: CSYSFN
PB Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic
DT Journal
LA English
AB A symposium report. **Desoctapeptideinsulin** (DOI), prepared by tryptic cleavage of porcine **insulin**, was utilized in the enzyme-catalyzed synthesis of human **insulin** analogs modified in the C-terminal region of the B-chain. The following four tetrapeptides, Gly-Phe-Phe-Phe-NH2 (1), Gly-Phe-Phe-N(Me)Phe-NH2 (2), Gly-Phe-Phe-N(Me)Tyr-NH2 (3) and Gly-Phe-N(Me)Phe-Phe-NH2 (4), were attached to the arginine (B22) carboxyl in DOI under TPCK-trypsin catalysis. DOI as well as the synthesized analogs were characterized by mass spectrum and amino acid anal. and their amino acid compns. were determined The effectivity of stimulation of C14-thymidine incorporation into DNA in pregnant mouse mammary gland explants was determined for two of the prepared **insulin** analogs containing peptides 1 and 3.
IT **11061-68-0DP**, Human **insulin**, N-methylated peptide bond analogs **275822-34-9P 275822-39-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(semisynthetic preparation of human **insulin** analogs containing N-methylated B24-B25 or B25-**B26** peptide bonds)
IT **39416-70-1P**, (1A-21A),(1B-22B)-**Insulin** (human)
RL: BPN (Biosynthetic preparation); RCT (Reactant); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(semisynthetic preparation of human **insulin** analogs containing N-methylated B24-B25 or B25-**B26** peptide bonds)
IT **275822-37-2P 275822-72-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(semisynthetic preparation of human **insulin** analogs containing N-methylated B24-B25 or B25-**B26** peptide bonds)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Casaretto, M	1987	368	709	Biol Chem Hoppe-Seyl	HCAPLUS

Jezek, J	1999	3	82	Collection Symposium	HCAPLUS
Lenz, V	1991	373	995	Biol Chem Hoppe-Seyl	
Mirmira, R	1989	264	6349	J Biol Chem	HCAPLUS
Nakagawa, S	1986	261	7332	J Biol Chem	HCAPLUS
Novakova, M	1997			Diploma Thesis. Char	

L14 ANSWER 3 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:205619 HCAPLUS
DN 133:4969
TI Preparation and characterization of analogs of tetrapeptide B23-**B26** and octapeptide B23-**B30** of human **insulin**
AU Jezek, Jan; Velek, Jiri; Velkova, Vlasta; Klasova, Lenka; Barthova, Jana; Ubik, Karel; Kasicka, Vaclav; Barth, Tomislav; Wollmer, Axel; Huml, Karel; Hauzerova, Linda; **Brandenburg, Dietrich**
CS Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Prague, 166 10, Czech Rep.
SO Collection Symposium Series (1999), 3(Biologically Active Peptides), 82-84
CODEN: CSYSFN
PB Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic
DT Journal
LA English
AB Using solid-phase synthesis, we prepared analogs of the C-terminal part of the B-chain of human **insulin**, i.e., the tetrapeptides Gly-Phe-Phe-Phe-NH2, Gly-Phe-Phe-N(Me)Phe-NH2, Gly-Phe-N(Me)Phe-Phe-NH2, and Gly-Phe-Phe-N(Me)Tyr-NH2 and octapeptides Gly-Phe-Phe-N(Me)Phe-Thr-Pro-Lys(Pac)-Thr-OH (Pac is a phenylacetyl residue) and Gly-Phe-Phe-Phe-Thr-Pro-Lys(Pac)-Thr-OH. The compds. were isolated by preparative HPLC and characterized by amino acid anal., mass spectrometry, capillary electrophoresis and anal. RP-HPLC.

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Barth, T	1993		745	Peptides 1992	HCAPLUS
Klasova, L	1999	3	85	Collection Symposium	HCAPLUS
Rohlena, J	1992			Thesis Charles Unive	
Svoboda, I	1994	375	373	Biol Chem Hoppe-Seyl	HCAPLUS
Svoboda, I	1996		75	Proc Czech-Taiwan Sy	

L14 ANSWER 4 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:578712 HCAPLUS
DN 132:45093
TI Receptor studies with novel **insulin** analogues and photoaffinity labelling techniques
AU **Brandenburg, D.**; Fabry, M.; Fischer, Y.; Gattner, H.-G.; Grotzinger, J.; Hagelstein, M.; **Havenith, C.**; Kurapkat, G.; Rutten, S.; Siedentop, M.; Wollmer, A.
CS Deutsches Wollforschungsinstitut an der RWTH Aachen, Aachen, D-52062, Germany
SO Peptide Science: Present and Future, Proceedings of the International Peptide Symposium, 1st, Kyoto, Nov. 30-Dec. 5, 1997 (1999), Meeting Date 1997, 223-225. Editor(s): Shimonishi, Yasutsugu. Publisher: Kluwer, Dordrecht, Neth.
CODEN: 68BYA5
DT Conference
LA English
AB The receptors for **insulin** and IGF-I show a high degree of homol., but different regions have been postulated for ligand binding. The authors' work aims at determining structure-function relationships, especially the structural requirements for receptor binding, and the definition of contact sites in the ligand-receptor binding regions. The authors have

replaced B26-tyrosine by D-alanine in **des-(B27-B30)insulin-B26**-amide (DTI) to give D-Ala-DT1 (1). The first and so far only antagonistic **insulin** analog is a **covalent insulin dimer.** To test whether the marked discrepancy between receptor binding and biopotency can be increased, they introduced binding-enhancing Arg residues into **insulin dimers** to give B29,B29'-suberoyl-(**ArgA0insulin**)2 (3) and B1,B1'-suberoyl-(**ArgA0insulin**)2 (5). D-Ala in position **B26** gives rise to a dramatic increase in receptor binding and in-vitro activity. The addition of Arg to B29,B29'-suberoyl **insulin dimer** (2) increased receptor binding but, unexpectedly, also activity. It is striking that 3 can elicit maximal **insulin** effect in cardiomyocytes but, like 2, is unable to do so in 3T3-L1 cells (53%). The authors conclude that the monomeric and **dimeric** analogs are interesting lead compds. for refined receptor/activity studies directed towards signal generation and transduction in various cell systems. Recombinant human IGF-I was acylated with Asa(4-azidosalicyloyl)-OSu. The 3 monosubstituted derivs. were subfractionated by RP-HPLC to give pure Nα-, NεB28-, and mixed NεB65/NεB68-Asa-IGF-I. Pure NαA1- and NεB29-Asa- **insulins** were prepared similarly. The radioiodinated probes could be specifically **crosslinked** to overexpressed receptors for **insulin**, IGF-I and 2 chimeric **insulin**/IGF-I receptors in 4 NIH3T3 cell lines. Tryptic digestion reveals characteristic labeling and fragmentation patterns which are currently analyzed further to determine the ligand-receptor contact sites.

IT **9004-10-8D**, **Insulin**, analogs, biological studies
9004-10-8D, **Insulin**, monomeric and **dimeric** analogs, biological studies **252723-56-1 252723-90-3 252723-93-6 252723-94-7**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(receptor studies with novel **insulin** analogs and photoaffinity labeling techniques)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Fabry, M	1966	7	65	BioMethods	
Leyer, S	1995	46	397	Int J Peptide Protei	HCAPLUS
Spoden, M	1995	6	221	Int J Peptide Protei	
Weiland, M	1990	87	1154	Proc Natl Acad Sci U	HCAPLUS

L14 ANSWER 5 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:187120 HCAPLUS
DN 130:347517
TI The solution structure of a superpotent B-chain-shortened single-replacement **insulin** analog
AU Kurapkat, Gunther; Siedentop, Michael; Gattner, Hans-Gregor; Hagelstein, Michael; **Brandenburg, Dietrich**; Grotzinger, Joachim; Wollmer, Axel
CS Institut fur Biochemie, Rheinisch-Westfalische Technische Hochschule Aachen, Aachen, D-52057, Germany
SO Protein Science (1999), 8(3), 499-508
CODEN: PRCIEI; ISSN: 0961-8368
PB Cambridge University Press
DT Journal
LA English
AB This paper reports on an **insulin** analog with 12.5-fold receptor affinity, the highest increase observed for a single replacement, and on its solution structure, determined by NMR spectroscopy. The analog is [D-AlaB26] **des-(B27-B30)-tetrapeptide-insulin-B26**-amide. C-terminal truncation of the B-chain by four (or five)

residues is known not to affect the functional properties of **insulin**, provided the new carboxylate charge is neutralized. As opposed to the dramatic increase in receptor affinity caused by the substitution of D-Ala for the wild-type residue TyrB26 in the truncated mol., this very substitution reduces it to only 18% of that of the wild-type hormone when the B-chain is present in full length. The **insulin** mol. in solution is visualized as an ensemble of conformers interrelated by a dynamic equilibrium The question is whether the "active" conformation of the hormone, sought after in innumerable structure/function studies, is or is not included in the accessible conformational space, so that it could be adopted also in the absence of the receptor. If there were any chance for the active conformation, or at least a predisposed state to be populated to a detectable extent, this chance should be best in the case of a superpotent analog. This was the motivation for the determination of the three-dimensional structure of [D-AlaB26] **des**-(B27-B30)-tetrapeptide-**insulin**-**B26**-amide. However, neither the NMR data nor CD spectroscopic comparison of a number of related analogs provided a clue concerning structural features predisposing **insulin** to high receptor affinity. After the present study it seems more likely than before that **insulin** will adopt its active conformation only when exposed to the force field of the receptor surface.

IT **224778-24-9P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(solution structure of a superpotent B-chain-shortened single-replacement **insulin** analog)

IT **9004-10-8**, **Insulin**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(solution structure of a superpotent B-chain-shortened single-replacement **insulin** analog in relation to the active conformation of **insulin**)

RETABLE

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)	Referenced File
Anderson, G	1964	86	1839	J Am Chem Soc	HCAPLUS
Baker, E	1988	319	369	Philos Trans R Soc L	HCAPLUS
Berendsen, H	1984	81	3684	J Chem Phys	HCAPLUS
Bi, R	1984	23	391	Biopolymers	HCAPLUS
Casaretto, M	1987	368	709	Biol Chem Hoppe Seyl	HCAPLUS
Chan, B	1988	241	1670	Science	HCAPLUS
Chen, G	1977	10	1195	Anal Lett	HCAPLUS
Crippen, G	1979	13	320	Int J Pept Protein R	HCAPLUS
Dai, I	1987	B30	55	Sci Sin	
de Meyts, P	1976	251	1877	J Biol Chem	HCAPLUS
de Meyts, P	1976		301	Methods in receptor	HCAPLUS
Delaglio, F	1995	6	277	J Biomol NMR	HCAPLUS
Derewenda, U	1991	220	425	J Mol Biol	HCAPLUS
Frost, S	1985	260	2646	J Biol Chem	HCAPLUS
Garrett, T	1998	394	395	Nature	HCAPLUS
Havel, T	1983	45	665	Bull Math Biol	
Hua, Q	1990	29	10545	Biochemistry	HCAPLUS
Hua, Q	1991	30	5505	Biochemistry	HCAPLUS
Hua, Q	1992	31	11940	Biochemistry	HCAPLUS
Hua, Q	1991	354	238	Nature	HCAPLUS
Hua, Q	1993	90	582	Proc Natl Acad Sci U	HCAPLUS
Hubbard, S	1994	372	746	Nature	HCAPLUS
Inouye, K	1979	101	752	J Am Chem Soc	
Johnson, B	1994	4	603	J Biomol NMR	HCAPLUS
Kaptein, R	1988	27	5389	Biochemistry	HCAPLUS
Konig, W	1970	103	788	Chem Ber	MEDLINE

Kristensen, S	1991	218	221	J Mol Biol	HCAPLUS
Kurapkat, G	1997	6	580	Protein Sci	HCAPLUS
Kurose, T	1994	269	29190	J Biol Chem	HCAPLUS
Lee, J	1994	266	C319	Am J Physiol	HCAPLUS
Lenz, V	1990			[Diplomarbeit] RWTH	
Leyer, S	1995	46	397	Int J Pept Protein R	HCAPLUS
Ludvigsen, S	1994	33	7998	Biochemistry	HCAPLUS
Ludvigsen, S	1998	279	1	J Mol Biol	HCAPLUS
Mirmira, R	1989	264	17613	J Biol Chem	
Mirmira, R	1989	264	6349	J Biol Chem	HCAPLUS
Mirmira, R	1991	266	1428	J Biol Chem	HCAPLUS
Moody, A	1974	6	12	Horm Metab Res	HCAPLUS
Murray-Rust, J	1992	14	325	Bioessays	HCAPLUS
Nakagawa, S	1992	31	3204	Biochemistry	HCAPLUS
Nakagawa, S	1986	261	7332	J Biol Chem	HCAPLUS
Olsen, H	1996	35	8836	Biochemistry	HCAPLUS
Pullen, R	1976	259	369	Nature	HCAPLUS
Scheek, R	1989	177	204	Methods Enzymol	HCAPLUS
Schwartz, G	1987	84	6408	Proc Natl Acad Sci U	HCAPLUS
Schwartz, G	1989	86	458	Proc Natl Acad Sci U	HCAPLUS
Shoelson, S	1993	268	4085	J Biol Chem	HCAPLUS
Siedentop, M	1997			[Dissertation] RWTH	
Sievert, D	1993		425	Chemistry of peptide	HCAPLUS
Sievert, D	1991			[Dissertation] RWTH	
Spackman, D	1958	30	1190	Analyst Chem	HCAPLUS
Spoden, M	1995	46	221	Int J Pept Protein R	HCAPLUS
Spoden, M	1988			[Dissertation] RWTH	
Waxman, E	1993	210	425	Anal Biochem	HCAPLUS
Wishart, D	1992	31	1647	Biochemistry	HCAPLUS
Wood, S	1975	55	531	Eur J Biochem	HCAPLUS
Wunsch, E	1974			Praparative methoden	
Wuthrich, K	1986			NMR of proteins and	

L14 ANSWER 6 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:696033 HCAPLUS
DN 126:19321
TI An enzymic-chemical synthesis of **insulins** with non-proteinogenic amino acid residues via chain condensation and subsequent disulfide folding
AU Lenz, V. J.; Leithaeuser, M.; Casaretto, M.; Gattner, H. G.; **Brandenburg, D.**; Hoecker, H.
CS Deutsches Wollforschungsinstitut, Aachen, D-52062, Germany
SO Peptides: Chemistry, Structure and Biology, Proceedings of the American Peptide Symposium, 14th, Columbus, Ohio, June 18-23, 1995 (1996), Meeting Date 1995, 637-638. Editor(s): Kaumaya, Pravin T. P.; Hodges, Robert S. Publisher: Mayflower Scientific, Kingswinford, UK.
CODEN: 63NTAF
DT Conference
LA English
AB A symposium report. [Tyr(NO2)A14,AbzB1]**des-B30** -single-chain **insulin** containing 2-aminobenzoic acid (Abz) and 3-nitrotyrosine was synthesized.
IT **9004-10-8DP**, **Insulin**, 2-aminobenzoic acid and 3-nitrotyrosine substituted analogs, preparation
RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of **insulins** with non-proteinogenic amino acid residues)

L14 ANSWER 7 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:906210 HCAPLUS
DN 123:330214
TI The role of the C-terminus of the **insulin** B-chain in modulating

structural and functional properties of the hormone
AU Leyer, Sigmar; Gattner, Hans-Gregor; Leithaeuser, Margot; **Brandenburg, Dietrich**; Wollmer, Axel; Hoecker, Hartwig
CS German Wool Res. Inst., Rheinisch-Westfaelische Technische Hochschule, Aachen, Germany
SO International Journal of Peptide & Protein Research (1995), 46(5), 397-407 CODEN: IJPPC3; ISSN: 0367-8377
PB Munksgaard
DT Journal
LA English
AB Within the scope of structure-function studies on the proteohormone **insulin**, the role of the C-terminal segment **B26-B30** for self-association and receptor interaction was analyzed. **Insulin** derivs. with modifications in the region **B26-B30** were synthesized by trypsin-catalyzed coupling reactions of **des**-(B23-B30)-**insulin** with synthetic peptides. The peptides were obtained by Fmoc solid-phase peptide synthesis. **Insulins** with multiple amino acid → glycine substitutions were examined to distinguish between the influence of the side chains and the influence of the main chain in positions **B27-B30** on the self-association of the hormone. The analogs [GlyB27,B28,B29,B30]**insulin** and [GlyB27,B28,**B30**] **insulin** exhibit relative receptor affinities of 80% and self-associate The successive extension of [AlaB26]**des**-(B27-B30)-**insulin-B26**-amide (relative receptor binding 273%) with amino acids corresponding to the native sequence **B27-B30** showed the influence of the length of the B-chain on receptor affinity: the extension by **B27**-threonine amide reduces receptor binding to 71%, all further prolongations have only small effects on the binding. The effect of the B28-side chain on main-chain conformation, self-association and receptor binding was examined with
[XB28]**des**-(B29-**B30**)-**insulin**-B28-amides (X = Phe, Gly, D-Pro). While the glycine and D-proline analogs (relative binding 104 and 143%, resp.) retain the self-association properties typical of **insulin**, [PheB28]**des**-(B29-**B30**)-**insulin**-B28-amide (relative binding 50%) shows diminished self-association The backbone-modified **insulin** derivative [SarB26]**des**-(B27-B30)-**insulin-B26**-amide (sarcosine = N-methylglycine) exhibits an unexpectedly high receptor affinity of 1100% which demonstrates that the **B26**-amide hydrogen of the native hormone is not important for receptor binding.

L14 ANSWER 8 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:198461 HCAPLUS
DN 122:1235
TI Residue **B26** modulates structural and functional properties of **des**-(B27-B30)-**insulins**
AU Sievert, D.; Lenz, V.; Gattner, H.-G.; **Brandenburg, D.**; Hoecker, H.; Wollmer, A.
CS Deutsches Wollforschungsinstitut, Aachen, D-5100, Germany
SO Chemistry of Peptides and Proteins (1993), 5/6(Pt. A), 425-32 CODEN: CHPPER; ISSN: 0723-6271
PB Verlag Mainz, Wissenschaftsverlag
DT Journal
LA English
AB The role of the invariant residue **B26**-tyrosine in determining structural and biol. properties of **insulin** has been studied using semisynthetic **des**(**B27-B30**)-**insulins** with modifications at **B26**. Various substitutions are readily accommodated during **insulin**-receptor interaction. A β-phenolic side chain and protection of the neg. charged α-carboxylate function of **B26** are prerequisite for

des(B27-B30)-**insulins** to **dimerize**. Analogs unable to **dimerize** can be fully or highly potent. The side chain in position **B26** serves to induce favorable main-chain adjustments rather than to contribute to direct hormone-receptor interactions.

IT **9004-10-8D, Insulin, des(B27-B30)** derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**insulin** structure and biol. activity in relation to residue **B26** of **des-(B27-B30)-insulins**)

L14 ANSWER 9 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:646596 HCAPLUS
DN 121:246596
TI Structure-activity relationship of **covalently dimerized insulin** derivatives: correlation of partial agonist efficacy with **cross-linkage** at lysine B29
AU Deppe, C.; Breiner, M.; **Brandenburg, D.**; Joost, H. G.
CS Inst. Pharmakologie Toxikologie der RWTH Aachen, Germany Deutsches Wollforschungsinstitut, Aachen, Germany
SO Naunyn-Schmiedeberg's Archives of Pharmacology (1994), 350(2), 213-17
CODEN: NSAPCC; ISSN: 0028-1298
DT Journal
LA English
AB The effects of 7 **covalently dimerized insulin** derivs. on glucose transport in differentiated 3T3-L1 cells were investigated. Sym. **cross-linkage** at lysine B29 with a **bridge** of 2 (oxalyl), 8 (suberoyl) or 12 (dodecanedioyl) carbon atoms produced derivs. with essentially unaltered receptor binding affinity but largely reduced intrinsic activity. Regardless of the chain length, these derivs. inhibited the effect of submaximal **insulin** concns. **Insulin** derivs. **cross-linked** at phenylalanine B1 or asym. at B1/B29 were full agonists of the **insulin** receptor. When lysine B29 was **cross-linked** with the inactive desoctapeptide(B23-**B30**) **insulin** at phenylalanine B1, the intrinsic activity of the resulting **dimer** was lower than that of **insulin**, but higher than that of the sym. B29-**dimers**. It is concluded that linkage at the B29-lysines, and not at the B1-phenylalanine, leads to partial agonism of **dimerized insulin** derivs., regardless of the length of the **crosslinker**.

IT **9004-10-8D, Insulin, dimers 75301-81-4 75301-82-5 75537-59-6 82047-72-1 82047-73-2 88402-09-9 88402-10-2**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(structure-activity of **covalently dimerized insulin** derivs.)

L14 ANSWER 10 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:622192 HCAPLUS
DN 121:222192
TI Semisynthetic **insulin** analogs modified in positions B24, B25 and B29
AU Svoboda, Ivan; **Brandenburg, Dietrich**; Barth, Tomislav; Gattner, Hans-Gregor; Jiracek, Jiri; Velek, Jiri; Blaha, Ivo; Ubik, Karel; Kasicka, Vaclav; et al.
CS Inst. Org. Chem. Biochem., Acad. Sci. Czech Republic, Prague, 16610, Czech Rep.
SO Biological Chemistry Hoppe-Seyler (1994), 375(6), 373-8
CODEN: BCHSEI; ISSN: 0177-3593

DT Journal
LA English
AB New semisynthetic analogs of human **insulin**, modified in the C-terminal region of the B-chain, were prepared to refine the authors' understanding of the importance of particular amino acid residues in the expression of hormone biol. properties. The following **insulin** analogs were synthesized by trypsin-catalyzed peptide-bond formation between the C-terminal arginineB22 of **des**-octapeptide(B23-B30)-**insulin** and synthetic octapeptides with the ε-amino group of lysineB29 protected by a phenylacetyl group: [L-Lys(Pac)B29]**insulin**, [D-PheB24,B25,L-Lys(Pac)B29] **insulin**, and [D-Phe(p-Et)B24,L-Lys(Pac)B29]**insulin**. Enzymic deprotection using immobilized penicillin amidohydrolase yielded: human **insulin**, [D-PheB24,B25]**insulin**, and [D-Phe(p-Et)B24]**insulin**. Biol. in vitro potencies (specific binding to cultured human lymphocytes IM-9 and lipogenic potency in isolated rat adipocytes) of the semisynthetic analogs were estimated, ranging from 0.2 to 100% relative to porcine **insulin**.
IT **11061-68-0**, Human **insulin** **12584-58-6**, Porcine **insulin** **39416-70-1**, **Des**(B23-30) **insulin** (human) **157184-76-4** **157184-77-5** **157184-78-6** **157184-79-7** **157184-80-0**
RL: BIOL (Biological study)
(lipogenic potency and receptor binding of, structure in relation to)

L14 ANSWER 11 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1994:236382 HCAPLUS
DN 120:236382
TI An **insulin** with the native sequence but virtually no activity
AU Wollmer, Axel; Gilge, Gabriele; **Brandenburg, Dietrich**; Gattner, Hans Gregor
CS Inst. Biochem., Rheinisch-Westfaelische Tech. Hochsch. Aachen, Aachen, D-52057, Germany
SO Biological Chemistry Hoppe-Seyler (1994), 375(3), 219-22
CODEN: BCHSEI; ISSN: 0177-3593
DT Journal
LA English
AB The B24-B25 peptide bond of **insulin** was replaced by an ester bond. To the authors' knowledge this is the first replacement of a main chain atom reported for the hormone. It is meant to eliminate a structurally important H-bond between the imino group of B25 and the carbonyl oxygen of A19, and consequently to enhance detachment of the C-terminal B chain from the underlying A chain. On the basis of independent exptl. evidence this very conformational change is believed to be a perrequisite for receptor binding. It was thus anticipated that increased flexibility would increase receptor binding and activity. Intriguingly, porcine [B24-B25 Co-O]**insulin** (depsi-**insulin**) and likewise [B24-B25 CO-O]**des**-(**B26**-**B30**)**insulin**-B25-amide (depsi-DPI-amide) were only 3-4% potent.
IT **9004-10-8**, **Insulin**, biological studies
9004-10-8D, **Insulin**, analog
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(biol. activity and conformation of)

L14 ANSWER 12 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:605368 HCAPLUS
DN 117:205368
TI Analysis of the human **insulin** receptor
AU Fabry, Marlies; **Brandenburg, Dietrich**
CS Dtsch. Wollforschungsinst., Tech. Hochsch. Aachen, Germany
SO Biological Chemistry Hoppe-Seyler (1992), 373(9), 915-23

CODEN: BCHSEI; ISSN: 0177-3593
DT Journal
LA English
AB The **insulin** derivative 4-azidosalicyloyl-[B1-biocytin-B2-lysine] **insulin** was used to photoaffinity-label the highly purified **insulin** receptor from human placenta. As shown by SDS-PAGE, the 5 monoiodo isomers, with iodine in positions B1, B16, **B26**, A14, or A19, gave different labeling patterns. After complete tryptic digestion of the **covalent** receptor complex with 125I-Asa-[BctB1,LysB2] **insulin**, a stable fragment of 18 kDa was isolated, which was further purified by HPLC. This tryptic fragment of the intact receptor corresponds, according to HPLC, Tricin-SDS-PAGE and 2D electrophoresis, to the similarly labeled sequenced domain of the receptor ectodomain (M. Fabry et al., 1992). Thus, **insulin** is bound to identical contact sites of native receptor and truncated ectodomain.
IT **9004-10-8, Insulin**, biological studies
RL: BIOL (Biological study)
(receptor for, **structure of binding domain of**)

L14 ANSWER 13 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:401060 HCAPLUS
DN 117:1060
TI Design and synthesis and a novel biotinylated photoreactive **insulin** for receptor analysis
AU Fabry, Marlies; **Brandenburg, Dietrich**
CS Dtsch. Wollforschungsinst., Aachen, W-5100, Germany
SO Biological Chemistry Hoppe-Seyler (1992), 373(3), 143-50
CODEN: BCHSEI; ISSN: 0177-3593
DT Journal
LA English
AB B1-(4-azido-salicyloyl)-[B1-biocytin,B2-lysine]**insulin** was synthesized by double Edman degradation of A1,B29-Msc2-**insulin** and stepwise acylation at the N-terminus of the B-chain. This derivative is homogeneous in reversed phase-HPLC and has a biol. in vitro activity of 20% and receptor binding of 15%, relative to **insulin.** Radioiodination and HPLC gave the B1-labeled 125I-derivative (I) as well as the 4 isomers with 125I-labeled tyrosine (A14,A19,B16,**B26**). UV-induced **crosslinking** of I with **insulin** receptors led to specific labeling of the α-subunit (Mr 130,000). The peptide bond LysB2-AspB3 is completely cleavable by trypsin (EC 3.4.21.4). I is thus a new tool for the anal. of the hormone-binding region by making possible the isolation of tryptic, biotinylated receptor fragments labeled by the dipeptide 125I-4-azidosalicyloyl-biocytinyl-Lys.
IT **65454-86-6 141639-22-7 141639-25-0 141668-34-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(biol. activity of)
IT **65742-92-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and Edmond degradation of)
IT **100754-44-7P 141639-24-9P 141639-28-3P 141639-29-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of)
IT **141639-26-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection of)
IT **141639-27-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)

(preparation and **insulin** receptor avidin labeling with)
IT 12584-58-6, Porcine **insulin**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with methylsulfonylethoxycarbonyl succinimidooxy ether)
IT 9004-10-8, **Insulin**, biological studies
RL: BIOL (Biological study)
(receptor for, determination of, by photoaffinity labeling)

L14 ANSWER 14 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1991:36119 HCAPLUS
DN 114:36119
TI In vivo metabolic activity of **des**-(**B26**-**B30**)-**insulin**-B25-amide and related analogs in the rat
AU Stuempel, Frank; Hartmann, Heinz; **Brandenburg, Dietrich**; Creutzfeldt, Werner
CS Dep. Med., Univ. Goettingen, Goettingen, D-3400, Germany
SO Diabetes Research and Clinical Practice (1990), 9(3), 257-64
CODEN: DRCPE9; ISSN: 0168-8227
DT Journal
LA English
AB Metabolic potency of **des**-(**B26**-**B30**)-**insulin**-B25-amide, [TyrB25]**des**-(**B26**-**B30**)-**insulin**-B25-amide, and [HisB25]**des**-(**B26**-**B30**)-**insulin**-B25-amide was studied in anesthetized rats. Compared to **insulin**, full potency for **des**-(B26-B30)-**insulin**-B25-amide and an enhanced potency for both substituted analogs was described previously on rat adipocytes in vitro. Hypoglycemic effects following i.v. injection of all analogs were almost identical to those of native **insulin** with a half-maximal ED of .apprx.3 nmol.kg-1. Stimulation of glucose metabolism during euglycemic **hyperinsulin**-/analogemic clamp studies was indistinguishable from that of the native hormone with a maximal stimulation of .apprx.19 mg.kg-1.min-1 and half-maximal effective hormone concns. of .apprx.1 pmol.mL-1. Analog action on individual peripheral tissues estimated by the uptake of 2-deoxyglucose as well as stimulation of lipogenesis in epididymal fat was not different than that of **insulin**. Thus, C-terminal amidation of **des**-(**B26**-**B30**)-**insulin** results in a shortened mol. with full in vivo metabolic potency. Addnl., substituting phenylalanine in position B25 by tyrosine or histidine preserve **insulin** potency.
IT **97123-35-8 103370-34-9 110353-31-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(biol. activity of, mol. structure in relation to)
IT 9004-10-8D, **Insulin**, analogs
RL: PRP (Properties)
(structure activity relations of)

L14 ANSWER 15 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1990:199075 HCAPLUS
DN 112:199075
TI Synthesis of A7,B7-**dicarbainsulin**, an analog with a noncleavable bond between A- and B-chain. II. Synthesis of the A-chain segments
AU Videnov, G.; Stoev, S.; **Brandenburg, Dietrich**
CS Inst. Mol. Biol., Sofia, 1113, Bulg.
SO Biological Chemistry Hoppe-Seyler (1989), 370(10), 1103-11
CODEN: BCHSEI; ISSN: 0177-3593
DT Journal
LA English
OS CASREACT 112:199075
AB As part of the total synthesis of [A7,B7-L,L-2,7-diaminosuberoyl]-**des**-(B26-B30)-**insulin** B25-amide, an **insulin** analog containing a noncleavable bond between A- and B-chain,

the chemical synthesis of the A-chain segments is described. The N-terminal sequence A(1-6), Boc-Gly-Ile-Val-Glu(OBu')-Gln-Cys(SBu')-NH-NH2, was synthesized in solution The middle segment A(8-16), Ddz-Thr(Bu')-Ser(Bu')-Ile-Cys(SBu')-Ser(Bu')-Leu-Tyr-(Bu')-Gln-Leu-NH-NH2, was obtained by solid phase synthesis according to the Fmoc strategy. The C-terminal segment A(17-21), Bpoc-Glu(OBu')-Asn-Tyr-Cys(Acm)-Asn-OBu', was prepared in solution

IT **9004-10-8DP, Insulin, A7,B7-dicarba analog**
RL: SPN (Synthetic preparation); PREP (Preparation)
(total synthesis of, preparation of A-chain fragments for)

L14 ANSWER 16 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:609172 HCAPLUS
DN 111:209172
TI Preparation of modified **insulins** as antidiabetic drugs
IN Spoden, Martin; Zahn, Helmut; **Brandenburg, Dietrich**; Creutzfeldt, Werner; Hartmann, Heinz
PA Fed. Rep. Ger.
SO Ger. Offen., 11 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 3727011	A1	19890223	DE 1987-3727011	19870813
PRAI DE 1987-3727011		19870813		

AB **Des**-(B25-B30)-hexapeptide **insulin** and the corresponding B24 amide, having C1-6 alkyl optionally substituted at the amide group, and Ph optionally substituted at the chain end, are prepared as drugs. The reaction of Boc2-**Des** (B23-**B30**) **insulin** with Gly-Phe-NH2, in the presence of trypsin and CaCl2, in glycerol, at pH 6.5, gave **Des**(B25-**B30**)hexapeptide **insulin** B24 amide (I). I had the same hypoglycemic activity than native **insulin**, in rats, however, the in vitro stimulation of glucose transport in rat adipocytes was much higher by native **insulin** than by I.

IT **39416-70-1 60825-48-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(peptide coupling of)

IT **39471-22-2P 103370-30-5P 123583-53-9P 123583-54-0P 123583-55-1P 123583-57-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antidiabetic drug)

L14 ANSWER 17 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:546933 HCAPLUS
DN 111:146933
TI Biological activity of **des**-(**B26-B30**)-**insulinamide** and related analogs in rat hepatocyte cultures
AU Hartmann, H.; Oberhaus, K.; Spahr, R.; **Brandenburg, D.**; Creutzfeldt, W.; Probst, I.
CS Dep. Med., Univ. Goettingen, Goettingen, Fed. Rep. Ger.
SO Diabetologia (1989), 32(7), 416-20
CODEN: DBTGAJ; ISSN: 0012-186X
DT Journal
LA English
AB Short-term and long-term biol. activities were studied in adult rat hepatocytes cultured in the presence of the **insulin** analogs **des**-(B26-B30)-**insulinamide**, [TyrB25] **des**-(B26-B30)-**insulinamide**, and [HisB25]**des**-(**B26-B30**)-**insulinamide**. When compared to **insulin**, full potency of **des**-(B26-B30)-**insulinamide** has been reported in rat

adipocytes and an enhanced potency has been reported for the other analogs. Steady state binding characteristics of the analogs to hepatocytes were indistinguishable from those of native **insulin** with half-maximal binding occurring at .apprx.0.8 nmol/L. Half-maximal effects for the stimulation of glycolysis and inhibition of basal and glucagon-activated glycogenolysis required identical concns. for **insulin** and all 3 analogs. Induction of the key glycolytic enzymes glucokinase and pyruvate kinase as well as the inhibition of glucagon-dependent induction of phosphenolpyruvate carboxykinase also required identical concns. of **insulin** and the 3 analogs. Apparently, in cultured hepatocytes the C-terminal amidation of **des**-(B26-B30)-**insulin** results in a mol. with full in vitro potency. In contrast to data obtained in adipocytes, the **des**-(**B26**-**B30**)-**insulin**-amidated analogs with tyrosine or histidine substitutions at position B25 are equally as potent as native **insulin** in eliciting biol. responses in rat hepatocyte culture.

IT **9004-10-8**, **Insulin**, biological studies
9004-10-8D, **Insulin**, analogs **97123-35-8**
103370-34-9 **110353-31-6**
RL: BIOL (Biological study)
(liver metabolism response to)

L14 ANSWER 18 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1989:436194 HCAPLUS
DN 111:36194
TI Hormone binding site of the **insulin** receptor: analysis using photoaffinity-mediated avidin complexing
AU Wedekind, Frank; Baer-Pontzen, Kristin; Bala-Mohan, Santosh; Choli, Dora; Zahn, Helmut; **Brandenburg, Dietrich**
CS Dtsch. Wollforschungsinst., Aachen, D-5100, Fed. Rep. Ger.
SO Biological Chemistry Hoppe-Seyler (1989), 370(3), 251-8
CODEN: BCHSEI; ISSN: 0177-3593
DT Journal
LA English
AB A trifunctional reagent was designed which allows derivatization of ligands, particularly peptides and proteins, for subsequent photoaffinity labeling of receptors and specific isolation of the **covalent** complex or its fragments. B29-(2-nitro-4-azidophenyl)-biocytinyl-**insulin** (NB-**insulin**) was synthesized, radioiodinated, and the **B26**-mono-iodo derivative isolated by HPLC. It was used to photoaffinity label human placental membranes and the purified **insulin** receptor. Extensive digestion of the **covalent** **insulin**-receptor complexes with trypsin (EC 3.4.21.4) led to the generation of a fragment of Mr 14,000. Specific complexing with avidin, derivatized avidin, or streptavidin could be demonstrated for the photoaffinity labeled α-subunit and the 14,000 core fragment. The latter was isolated (.apprx.100 pmol from 3-4 placentae) by streptavidin affinity chromatog. and HPLC. According to microsequencing based on the known primary structure of the **insulin** receptor, the N-terminus of the core peptide appears to be Leu20-His21-Glu22-Leu23. Thus, a part of the **insulin**-binding region of the receptor is located close to the N-terminus of its α-subunit in a remarkably stable domain of the sequence 20-(approx.) 120.

IT **12584-58-6**
RL: RCT (Reactant); RACT (Reactant or reagent)
(iodination of, for photoaffinity labeling of placental membrane of humans and **insulin** receptor)

IT **121396-31-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and radioiodination of)

IT **121396-29-0**

RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with azidonitrophenylbiocytin nitrophenyl ester)
IT **9004-10-8**, **Insulin**, biological studies
RL: BIOL (Biological study)
(receptors for, hormone binding site of, anal. of)

L14 ANSWER 19 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1988:38409 HCAPLUS
DN 108:38409
TI New photo-reactive derivatives of **insulin** for affinity-labeling of the **insulin** receptor
AU Ambrosius, D.; Bala-Mohan, S.; Behrendt, C.; Schaefer, K.; Schuettler, A.; **Brandenburg, D.**
CS Dtsch. Wollforschungsinst., Aachen, D-5100, Fed. Rep. Ger.
SO Pept., Proc. Eur. Pept. Symp., 19th (1987), Meeting Date 1986, 521-3. Editor(s): Theodoropoulos, Dimitrios. Publisher: de Gruyter, Berlin, Fed. Rep. Ger.
CODEN: 56ABA8
DT Conference
LA English
AB A symposium on enzyme-catalyzed semisynthesis of **des**-(**B26-B30**)-**insulin**-B25-(4-Nap-iminoethyleneamide) and of a bivalent **dimeric photoinsulin.**
IT **9004-10-8DP**, **Insulin**, photoreactive derivs.
RL: SPN (Synthetic preparation); PREP (Preparation)
(semisynthesis of, for photo-labeling of **insulin** receptor)

L14 ANSWER 20 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:527328 HCAPLUS
DN 107:127328
TI Shortened **insulin** with enhanced in vitro potency
AU Casaretto, Monika; Spoden, Martin; Diaconescu, Cornelia; Gattner, Hans Gregor; Zahn, Helmut; **Brandenburg, Dietrich**; Wollmer, Axel
CS Dtsch. Wollforschungsinst., Aachen, D-5100, Fed. Rep. Ger.
SO Biological Chemistry Hoppe-Seyler (1987), 368(6), 709-16
CODEN: BCHSEI; ISSN: 0177-3593
DT Journal
LA English
AB Although removal of residues **B26-B30** leaves **insulin** with full biol. activity, provided the new C-terminus is amidated (W.H. Fischer et al., 1985), it was shown that it does not preclude enhancement of potency. Seven analogs of **des**-(**B26-B30**)-**insulin**-B25-amide were prepared by trypsin-mediated semisynthesis, the replacements being D-PheB24; HisB25, D-PheB25, TrpB25, TyrB25; D-PheB24,B25 and D-PheB24, TyrB25. Mere conversion of the configuration of B25-phenylalanine reduces in vitro potency to 0.5%. If B25-phenylalanine is, however, substituted by histidine or tyrosine, activity is increased to 310 or 230%, resp. According to the features common to these 2 side chains, the favorable effect should be due to their ring structure with balanced aromatic and polar or H-bonding properties, resp. In the complete **insulin** mol., the C-terminal pentapeptide modulates the subtle role that residues B24 and/or B25 play in receptor binding and activity; its presence may have a pos. or neg. effect. The drastic difference in activity between the shortened analogs are in no way reflected in the CD spectra which are very similar, though clearly different from that of native **insulin.**
IT **9004-10-8DP**, **Insulin**, analogs **97123-35-8DP**, analogs **103370-34-9P 110341-94-1P 110341-95-2P 110341-96-3P 110341-97-4P 110341-98-5P 110353-31-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and biopotency of)

IT 60825-48-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deprotection of)

L14 ANSWER 21 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:27882 HCAPLUS
DN 106:27882
TI Structure-function relationships of shortened [LeuB25]**insulins**, semisynthetic analogs of a mutant human **insulin**
AU Fischer, Wolfgang H.; Saunders, Derek; **Brandenburg, Dietrich**; Diaconescu, Cornelia; Wollmer, Axel; Dodson, Guy; De Meyts, Pierre; Zahn, Helmut
CS Dtsch. Wollforschungsinst., Aachen, Fed. Rep. Ger.
SO Biological Chemistry Hoppe-Seyler (1986), 367(9), 999-1006
CODEN: BCHSEI; ISSN: 0177-3593
DT Journal
LA English
AB Replacement of B25-phenylalanine by leucine in the **insulin** sequence causes marked inactivation. The effect of this sequence variation was studied in **des**-(**B26**-30)-**insulin** . Human [LeuB25]**des**-(**B26**-30)-**insulin** [105953-60-4] and its B25-amide [**103370-33-8**] were prepared by trypsin-mediated semisynthesis from N-terminally protected **des**-(B23-30)-**insulin** and synthetic tripeptides. The relative lipogenic potency in isolated rat adipocytes was 8.0% for the truncated analog with a free B25-carboxyl function, and 18.1% for the amidated analog. Binding to cultured human IM-9 lymphocytes was 4% and 9%, resp. Thus, both shortened **insulins** are markedly more active than human [LeuB25]**insulin** [**105953-62-6**]. The PheB25 → LeuB25 substitution in both the shortened and the full sequence has a moderate effect on the CD spectrum, indicating that the gross main chain conformation is largely retained in both mols. Independent of the substitution an absolute increase of the CD is observed on amidation of the B25-carboxyl group.
IT 78564-74-6
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(biol. activity of, of human, structure in relation to)
IT 60825-48-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling of, with tripeptide amide)
IT 88506-01-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(coupling of, with tripeptidebutyl ester)
IT 103370-33-8P 105953-60-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of, of human, structure in relation to)
IT 105953-61-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis of)

L14 ANSWER 22 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1985:432426 HCAPLUS
DN 103:32426
TI A shortened **insulin** with full in vitro potency
AU Fischer, Wolfgang H.; Saunders, Derek; **Brandenburg, Dietrich**; Wollmer, Axel; Zahn, Helmut
CS Dtsch. Wollforschungsinst., Rheinisch-Westfael. Tech. Hochsch. Aachen, Aachen, D-5100, Fed. Rep. Ger.

SO Biological Chemistry Hoppe-Seyler (1985), 366(5), 521-5
CODEN: BCHSEI; ISSN: 0177-3593
DT Journal
LA English
AB **Des**[(B26-30)-pentapeptide]**insulin**-B25-amide [97123-35-8] was prepared from protected **des**-[(B23-30)-octapeptide]**insulin** (pig) and Gly-Phe-Phe-NH2 [34367-79-8] by trypsin-mediated semisynthesis in a yield of 9% (based on **insulin**). The analog was characterized with respect to chemical, biol. function, and CD spectroscopy. Whereas **des**[(**B26**-30)-pentapeptide]**insulin** [55599-09-2] with free carboxylate group exhibited a typical **insulin** activity of only 25% in vitro, **des**[(**B26**-30)-pentapeptide]**insulinamide** was fully active. Therefore **des**[(**B26**-30)-pentapeptide]**insulin** meets all structural and dynamic requirements for recognition and binding of the receptor as well as exertion of the biol. effect, provided that the neg. charge in the hydrophobic environment of PheB25 is neutralized.
IT 55599-09-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(biol. activity of, amide form in relation to)
IT 97123-35-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of)
IT 60825-48-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with glycyldiphenylamide)

L14 ANSWER 23 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1983:89861 HCAPLUS
DN 98:89861
TI Preparation and properties of **crosslinked insulins** containing a split peptide bond
AU Wang, Chihchen; Chu, Shangchuan; **Brandenburg, Dietrich**; Wollmer, Axel
CS Inst. Biophys., Acad. Sin., Peking, Peop. Rep. China
SO Pept., Proc. Eur. Pept. Symp., 16th (1981), Meeting Date 1980, 389-94. Editor(s): Brunfeldt, K. Publisher: Scriptor, Copenhagen, Den.
CODEN: 48NWA3
DT Conference
LA English
AB A1-B29-CMB-**insulin** (I, CMB = carbonylbismethionyl) was cleaved at the ArgB22-GlyB23 peptide bond by trypsin to give A1-B29-CMB-**insulin** with a split B22/23 bond. B1-Msc-DPI [Msc = MeSO2CH2CH2O2C, DPI = **des**-pentapeptide(**B26**-30)-**insulin**] was treated with CMB-(OC6H4NO2-p)2 and then coupled with Msc-Tyr-Thr-Pro-Lys-Ala-OH to give the protected **insulin**, which was deblocked to give A1-B29-CMB-**insulin** with a split B25/26 bond. The biol. activity of the split **insulins** are lower than that of I. The split **insulins** differ markedly from I in their CD spectrum; the split **insulins** have not kept the original conformation of I.
IT 53800-33-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(cleavage of, by trypsin)
IT 84134-81-6
RL: RCT (Reactant); RACT (Reactant or reagent)
(**crosslinking** of, with carbonylbismethionine bis(nitrophenyl) ester)
IT 9004-10-8DP, **crosslinked** derivs. containing split peptide

bonds 79620-22-7P **84683-83-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and CD and biol. activity of)
IT **84683-81-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of)
IT **84683-85-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and deblocking and biol. activity of)
IT **84683-86-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deblocking of)
IT **84683-82-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and peptide coupling of, with pentapeptide derivative)
IT **84683-84-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and tryptic cleavage of)

L14 ANSWER 24 OF 24 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1983:54445 HCAPLUS
DN 98:54445
TI Preparation and properties of **des**-pentapeptide (26-30) **insulin** analogs
AU Chu, Shangchuan; Wang, Chihchen; **Brandenburg, Dietrich**
CS Inst. Biochem., Acad. Sin., Shanghai, Peop. Rep. China
SO Pept., Proc. Eur. Pept. Symp., 16th (1981), Meeting Date 1980, 359-64. Editor(s): Brunfeldt, K. Publisher: Scriptor, Copenhagen, Den. CODEN: 48NWA3
DT Conference
LA English
AB A1,B29-(Boc)2-**insulin** (Boc = Me3CO2C) was acylated with Msc-ONSu (Msc = MeSO2CH2CH2O2C, NSu = succinimido) and then deblocked by CF3CO2H to give B1-Msc-**insulin**, which was cleaved by pepsin to give B1-Msc-DPI [DPI = **des**-pentapeptide-(**B26**-30)-**insulin**], which was used in the semisynthesis of DPI analogs. B1-Msc-DPI was coupled with Boc-Lys(Boc)-OC6H4NO2-p to give the protected **insulin**, which was Boc-deblocked by CF3CO2H and then Msc-deblocked by NaOH to give LysA0-DPI. B1-Msc-DPI underwent the Edman degradation to give B1-Msc-**des**-GlyA1-DPI (I), which was Msc-deblocked by NaOH to give **des**-GlyA1-DPI. I was coupled with Msc-Ala-OC6H4NO2-p and then Msc-deblocked to give [AlaA1]-DPI. [D-AlaA1]-DPI was prepared similarly from I and Msc-D-Ala-OC6H4NO2-p. Variations at the N-terminal glycine caused redns. of biol. activity which were similar to those for the corresponding **insulin** analogs.
IT 39302-19-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(characterization and biol. activity of)
IT 11137-90-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(methylsulfonylethoxycarbonylation of)
IT **84134-76-9P 84134-77-0P 84134-78-1P**
84134-82-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of)
IT **84134-79-2P 84134-83-8P 84134-84-9P**
84134-86-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and deblocking of)

IT 63304-64-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and pepsin-catalyzed cleavage of)

IT 84134-81-6P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and peptide coupling reaction and Edman degradation of)

IT 9004-10-8DP, des-pentapeptide-(β26-30) analogs
RL: PREP (Preparation)
(semisynthesis and biol. activity of)

=>

```
=> d sta que l34
L32         1905 SEA FILE=REGISTRY ABB=ON  PLU=ON  GIVEQCCTSICSLYQLENYCN/SQSP
L33         2325 SEA FILE=REGISTRY ABB=ON  PLU=ON  FVNQHLCGSHLVEALYLVCGERGFF/SQS
                 P
L34         1300 SEA FILE=REGISTRY ABB=ON  PLU=ON  L32 AND L33


=> d his

     (FILE 'HOME' ENTERED AT 07:06:45 ON 25 MAY 2004)
                 SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 07:06:55 ON 25 MAY 2004
L1             1 S US20020160938/PN OR (WO2000-EP1530 OR DE99-19908041)/AP,PRN
                 E HOECKER H/AU
                 E BRANDENBURG D/AU
L2           277 S E3-E5,E7-E10
                 E HAVENITH C/AU
L3             9 S E3-E4,E6
                 E AVENTI/PA,CS
L4          2089 S E4-E6 OR AVENTIS?/PA,CS

     FILE 'REGISTRY' ENTERED AT 07:09:52 ON 25 MAY 2004
L5             1 S 9004-10-8
L6             1 S 11061-68-0
L7          7097 S INSULIN
L8          7095 S L7 NOT L5,L6

     FILE 'HCAPLUS' ENTERED AT 07:10:06 ON 25 MAY 2004
L9         97354 S L5 OR L6
L10        34776 S L8
L11       164855 S ?INSULIN?
L12            1 S L1 AND L9-L11
L13          359 S L2-L4 AND L9-L11
L14           30 S L13 AND ?DIMER?
L15            4 S L14 AND ?BRIDG?
L16           14 S L14 AND ?COVALEN?
L17           13 S L14 AND (?CROSSLINK? OR ?CROSS LINK?)
L18           20 S L15-L17
L19           10 S L14 NOT L18
L20            4 S L14 AND DES
L21            4 S L14 AND (B27 OR B30 OR B26)
L22            5 S L20,L21
L23            5 S L22 AND L15-L19
L24            6 S L12,L23
L25           24 S L14-L19 NOT L24
                 SEL RN L12

     FILE 'REGISTRY' ENTERED AT 07:17:29 ON 25 MAY 2004
L26           18 S E1-E18
L27            2 S L26 AND L5,L6
L28           11 S L26 AND L8
L29            5 S L26 NOT L27,L28
L30            3 S L28 AND S>=12
L31            8 S L28 NOT L30
L32         1905 S GIVEQCCTSICSLYQLENYCN/SQSP
L33         2325 S FVNQHLCGSHLVEALYLVCGERGFF/SQSP
L34         1300 S L32 AND L33
L35          920 S L34 AND MULTICHAIN/NTE
L36          912 S L35 AND DISULFIDE BRIDGE/NTE
L37            3 S L35 AND SULFIDE BRIDGE/NTE
L38           24 S L35 AND COVALENT BRIDGE/NTE
L39           67 S L35 AND AMIDE BRIDGE/NTE
```

```
L40          920 S L36-L39
L41           10 S L26 AND L34
L42            2 S L28 NOT L41
L43            1 S L42 NOT 39416-70-1
L44           11 S L41,L43

     FILE 'HCAPLUS' ENTERED AT 07:25:30 ON 25 MAY 2004

     FILE 'REGISTRY' ENTERED AT 07:25:39 ON 25 MAY 2004
L45           10 S L44 NOT L27

     FILE 'HCAPLUS' ENTERED AT 07:25:57 ON 25 MAY 2004
L46            2 S L45
L47         1461 S L40

     FILE 'REGISTRY' ENTERED AT 07:26:19 ON 25 MAY 2004
L48          919 S L47 NOT L5,L6

     FILE 'HCAPLUS' ENTERED AT 07:26:32 ON 25 MAY 2004
L49         1108 S L48

     FILE 'REGISTRY' ENTERED AT 07:26:42 ON 25 MAY 2004
L50           12 S L48 AND S>=12

     FILE 'HCAPLUS' ENTERED AT 07:27:47 ON 25 MAY 2004
L51            5 S L50
L52            6 S L46,L51
L53            2 S L52 AND L1-L4,L12-L25

     FILE 'REGISTRY' ENTERED AT 07:28:47 ON 25 MAY 2004
L54            1 S 170712-62-6

     FILE 'HCAPLUS' ENTERED AT 07:28:54 ON 25 MAY 2004
L55            4 S L52 NOT L53
L56            4 S L55 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
                 SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 07:31:41 ON 25 MAY 2004
L57            9 S E19-E27
L58            4 S L57 AND (C290H445N67O80S12 OR C264H397N67O97S12 OR C265H400N6
L59          900 S L40 AND CYS 7/NTE
L60          848 S L59 AND CYS 19/NTE
L61          806 S L60 AND CYS 6/NTE
L62           11 S L61 AND PHE 1/NTE
L63            3 S L61 AND SAR 26/NTE
L64           13 S L62,L63
L65           12 S L64 NOT FE/ELS
L66            7 S L65 NOT L45
L67            3 S L66 NOT TERMINAL MOD/NTE
L68            3 S L66 NOT TERMINAL MOD/NTE

     FILE 'HCAPLUS' ENTERED AT 07:42:24 ON 25 MAY 2004
L69            2 S L68
L70            4 S L46,L69
L71            4 S L70 AND L1-L4,L9-L25
L72          811 S L49 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
L73           41 S L72 AND ?DIMER?
L74           29 S L72 AND ?COVALEN?
L75           13 S L72 AND ?BRIDG?
L76           35 S L72 AND (?DISULFID? OR ?DISULPHID?)
L77           96 S L73-L76
L78           95 S L77 AND L9,L11
L79           18 S L78 AND P/DT
```

```
L80            2 S L79 AND (SARB26 OR SAR B26 OR B27 OR B30 OR B26 OR SARCOSIN?)
L81            1 S L78 AND DES B27
L82            1 S L80 AND L81
L83            5 S L71,L82
L84            4 S L83 NOT L1
                 SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 07:49:31 ON 25 MAY 2004
L85           41 S E28-E68
L86            3 S L85 AND L68
                 SEL RN 1
L87            2 S L86 NOT E69
L88            1 S L85 AND L45
L89            3 S L87,L88
L90           38 S L85 NOT L89
L91           10 S L90 AND 30B
L92            2 S L90 AND 26B
L93            1 S L92 NOT 25B
                 SEL RN L91 4 5
L94            2 S E70-E71
L95            6 S L93,L94,L89
L96            3 S L95 NOT 29B
L97            3 S L95 NOT L96
L98            2 S L96 NOT 117924-56-8
                 SEL RN L97 3
L99            1 S E72
L100           2 S L98,L88

     FILE 'HCAPLUS' ENTERED AT 08:01:05 ON 25 MAY 2004
L101           3 S L100
L102           3 S L46,L101
L103          29 S L14-L25 NOT L102
L104          28 S L103 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)

=> fil hcaplus
FILE 'HCAPLUS' ENTERED AT 08:03:12 ON 25 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)
```



```
FILE COVERS 1907 - 25 May 2004  VOL 140 ISS 22
FILE LAST UPDATED: 24 May 2004  (20040524/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
 => d l105 all tot

L105 ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2000:608776  HCAPLUS
DN   133:203411
ED   Entered STN:  01 Sep 2000
TI   Covalently bridged insulin dimers
```

IN Hoecker, Hartwig; **Havenith, Chantalle**; **Brandenburg, Dietrich**
PA **Aventis Pharma Deutschland G.m.b.H., Germany**
SO PCT Int. Appl., 22 pp.
CODEN: PIXXD2
DT **Patent**
LA German
IC ICM C07K014-62
ICS G01N033-74; A61K038-28; A61P005-48
CC 2-6 (Mammalian Hormones)
Section cross-reference(s): 34
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
PI	WO 2000050456	A2	20000831	WO 2000-EP1530	20000224	<--
	WO 2000050456	A3	20001207			
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
	EP 1161452	A2	20011212	EP 2000-909247	20000224	<--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
	JP 2003525864	T2	20030902	JP 2000-601034	20000224	<--
	AU 765076	B2	20030911	AU 2000-31601	20000224	<--
	US 2002160938	A1	20021031	US 2001-934766	20010823	<--
	ZA 2001006971	A	20021122	ZA 2001-6971	20010823	<--
PRAI	DE 1999-19908041	A	19990224	<--		
	WO 2000-EP1530	W	20000224	<--		

OS MARPAT 133:203411
AB Modified **insulin dimers** are prepared in which the α-amino groups of the Phe1 residues of the 2 B chains are joined with C(O)(CRR')nC(O) [R, R' = H, NH2, C1-10 alkyl, (substituted) aryl; n = 0-16] and residues 26-30 of the 2 B chains are replaced with X [X = C1-10 alkyl, (substituted) aryl, (substituted) aryloxy, amino acid, NRR'] for use in medicaments for treatment of diabetes. The **dimers** are synthesized from the corresponding monomers (prepared enzymically or by genetic engineering methods) by provision with protecting groups as needed and reaction with an activated dicarboxylic acid. The **dimers** show high affinity for **insulin** receptors, very high biol. activity, and selectivity for the liver.
ST **insulin dimer** prepn dicarboxylate; receptor affinity **insulin dimer**
IT Diagnosis
(agents; **covalently bridged insulin dimers**)
IT Antidiabetic agents
(**covalently bridged insulin dimers**)
IT Carboxylic acids, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(dicarboxylic; **covalently bridged insulin dimers**)
IT Liver
(**insulin dimers** with specificity for; **covalently bridged insulin dimers**)
IT **9004-10-8DP**, **Insulin**, **dimers**, biological

studies 224778-24-9DP, **dimers 290292-50-1DP**, **dimers 290292-63-6DP**, **dimers 290292-66-9P 290292-91-0P 290292-93-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**covalently bridged insulin dimers**)

IT **11061-68-0**, Human **insulin** 57903-15-8 68528-80-3 289909-34-8 289909-35-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(**covalently bridged insulin dimers**)

IT **39416-70-1P**, (1A-21A),(1B-22B)-**Insulin** (human)
170712-62-6P **290292-50-1P 290292-65-8P 290292-67-0P 290292-92-1P 290293-08-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**covalently bridged insulin dimers**)

L105 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1999:187120 HCAPLUS
DN 130:347517
ED Entered STN: 23 Mar 1999
TI The solution structure of a superpotent B-chain-shortened single-replacement **insulin** analog
AU Kurapkat, Gunther; Siedentop, Michael; Gattner, Hans-Gregor; Hagelstein, Michael; **Brandenburg, Dietrich**; Grotzinger, Joachim; Wollmer, Axel
CS Institut fur Biochemie, Rheinisch-Westfalische Technische Hochschule Aachen, Aachen, D-52057, Germany
SO Protein Science (**1999**), 8(3), 499-508
CODEN: PRCIEI; ISSN: 0961-8368
PB Cambridge University Press
DT Journal
LA English
CC 2-2 (Mammalian Hormones)
AB This paper reports on an **insulin** analog with 12.5-fold receptor affinity, the highest increase observed for a single replacement, and on its solution structure, determined by NMR spectroscopy. The analog is [D-AlaB26]des-(B27-B30)-tetrapeptide-**insulin**-B26-amide. C-terminal truncation of the B-chain by four (or five) residues is known not to affect the functional properties of **insulin**, provided the new carboxylate charge is neutralized. As opposed to the dramatic increase in receptor affinity caused by the substitution of D-Ala for the wild-type residue TyrB26 in the truncated mol., this very substitution reduces it to only 18% of that of the wild-type hormone when the B-chain is present in full length. The **insulin** mol. in solution is visualized as an ensemble of conformers interrelated by a dynamic equilibrium The question is whether the "active" conformation of the hormone, sought after in innumerable structure/function studies, is or is not included in the accessible conformational space, so that it could be adopted also in the absence of the receptor. If there were any chance for the active conformation, or at least a predisposed state to be populated to a detectable extent, this chance should be best in the case of a superpotent analog. This was the motivation for the determination of the three-dimensional structure of [D-AlaB26]des-(B27-B30)-tetrapeptide-**insulin**-B26-amide. However, neither the NMR data nor CD spectroscopic comparison of a number of related analogs provided a clue concerning structural features predisposing **insulin** to high receptor affinity. After the present study it seems more likely than before that **insulin** will adopt its active conformation only when exposed to the force field of the

receptor surface.
ST soln structure superpotent **insulin** analog
IT Secondary structure
Tertiary structure
(protein; solution structure of a superpotent B-chain-shortened single-replacement **insulin** analog)
IT Solution structure
(solution structure of a superpotent B-chain-shortened single-replacement **insulin** analog)
IT **Insulin** receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(solution structure of a superpotent B-chain-shortened single-replacement **insulin** analog in relation to the active conformation of **insulin**)
IT **224778-24-9P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(solution structure of a superpotent B-chain-shortened single-replacement **insulin** analog)
IT **9004-10-8**, **Insulin**, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(solution structure of a superpotent B-chain-shortened single-replacement **insulin** analog in relation to the active conformation of **insulin**)
RE.CNT 58 THERE ARE 58 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anderson, G; J Am Chem Soc 1964, V86, P1839 HCAPLUS
(2) Baker, E; Philos Trans R Soc Lond B Biol Sci 1988, V319, P369 HCAPLUS
(3) Berendsen, H; J Chem Phys 1984, V81, P3684 HCAPLUS
(4) Bi, R; Biopolymers 1984, V23, P391 HCAPLUS
(5) Casaretto, M; Biol Chem Hoppe Seyler 1987, V368, P709 HCAPLUS
(6) Chan, B; Science 1988, V241, P1670 HCAPLUS
(7) Chen, G; Anal Lett 1977, V10, P1195 HCAPLUS
(8) Crippen, G; Int J Pept Protein Res 1979, V13, P320 HCAPLUS
(9) Dai, I; Sci Sin 1987, VB30, P55
(10) de Meyts, P; J Biol Chem 1976, V251, P1877 HCAPLUS
(11) de Meyts, P; Methods in receptor research I 1976, P301 HCAPLUS
(12) Delaglio, F; J Biomol NMR 1995, V6, P277 HCAPLUS
(13) Derewenda, U; J Mol Biol 1991, V220, P425 HCAPLUS
(14) Frost, S; J Biol Chem 1985, V260, P2646 HCAPLUS
(15) Garrett, T; Nature 1998, V394, P395 HCAPLUS
(16) Havel, T; Bull Math Biol 1983, V45, P665
(17) Hua, Q; Biochemistry 1990, V29, P10545 HCAPLUS
(18) Hua, Q; Biochemistry 1991, V30, P5505 HCAPLUS
(19) Hua, Q; Biochemistry 1992, V31, P11940 HCAPLUS
(20) Hua, Q; Nature 1991, V354, P238 HCAPLUS
(21) Hua, Q; Proc Natl Acad Sci USA 1993, V90, P582 HCAPLUS
(22) Hubbard, S; Nature 1994, V372, P746 HCAPLUS
(23) Inouye, K; J Am Chem Soc 1979, V101, P752
(24) Johnson, B; J Biomol NMR 1994, V4, P603 HCAPLUS
(25) Kaptein, R; Biochemistry 1988, V27, P5389 HCAPLUS
(26) Konig, W; Chem Ber 1970, V103, P788 MEDLINE
(27) Kristensen, S; J Mol Biol 1991, V218, P221 HCAPLUS
(28) Kurapkat, G; Protein Sci 1997, V6, P580 HCAPLUS
(29) Kurose, T; J Biol Chem 1994, V269, P29190 HCAPLUS
(30) Lee, J; Am J Physiol 1994, V266, PC319 HCAPLUS
(31) Lenz, V; [Diplomarbeit] RWTH Aachen 1990
(32) Leyer, S; Int J Pept Protein Res 1995, V46, P397 HCAPLUS
(33) Ludvigsen, S; Biochemistry 1994, V33, P7998 HCAPLUS
(34) Ludvigsen, S; J Mol Biol 1998, V279, P1 HCAPLUS
(35) Mirmira, R; J Biol Chem 1989, V264, P17613
(36) Mirmira, R; J Biol Chem 1989, V264, P6349 HCAPLUS

(37) Mirmira, R; J Biol Chem 1991, V266, P1428 HCAPLUS
(38) Moody, A; Horm Metab Res 1974, V6, P12 HCAPLUS
(39) Murray-Rust, J; Bioessays 1992, V14, P325 HCAPLUS
(40) Nakagawa, S; Biochemistry 1992, V31, P3204 HCAPLUS
(41) Nakagawa, S; J Biol Chem 1986, V261, P7332 HCAPLUS
(42) Olsen, H; Biochemistry 1996, V35, P8836 HCAPLUS
(43) Pullen, R; Nature 1976, V259, P369 HCAPLUS
(44) Scheek, R; Methods Enzymol 1989, V177, P204 HCAPLUS
(45) Schwartz, G; Proc Natl Acad Sci USA 1987, V84, P6408 HCAPLUS
(46) Schwartz, G; Proc Natl Acad Sci USA 1989, V86, P458 HCAPLUS
(47) Shoelson, S; J Biol Chem 1993, V268, P4085 HCAPLUS
(48) Siedentop, M; [Dissertation] RWTH Aachen 1997
(49) Sievert, D; Chemistry of peptides and proteins Aachen:Wissenschaftsverlag Mainz 1993, P425 HCAPLUS
(50) Sievert, D; [Dissertation] RWTH Aachen 1991
(51) Spackman, D; Analyst Chem 1958, V30, P1190 HCAPLUS
(52) Spoden, M; Int J Pept Protein Res 1995, V46, P221 HCAPLUS
(53) Spoden, M; [Dissertation] RWTH Aachen 1988
(54) Waxman, E; Anal Biochem 1993, V210, P425 HCAPLUS
(55) Wishart, D; Biochemistry 1992, V31, P1647 HCAPLUS
(56) Wood, S; Eur J Biochem 1975, V55, P531 HCAPLUS
(57) Wunsch, E; Praparative methoden in der organischen chemie 1974
(58) Wuthrich, K; NMR of proteins and nucleic acids 1986

L105 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:540900 HCAPLUS
DN 125:196368
ED Entered STN: 11 Sep 1996
TI Natural Peptides as Building Blocks for the Synthesis of Large Protein-like Molecules with Hydrazone and Oxime Linkages
AU Rose, Keith; Zeng, Weiguang; Regamey, Pierre-Olivier; Chernushevich, Igor V.; Standing, Kenneth G.; Gaertner, Hubert F.
CS Department of Medical Biochemistry, University Medical Center, Geneva, 1211, Switz.
SO Bioconjugate Chemistry (**1996**), 7(5), 552-556
CODEN: BCCHES; ISSN: 1043-1802
PB American Chemical Society
DT Journal
LA English
CC 34-4 (Amino Acids, Peptides, and Proteins)
AB Methods are known for the production of synthetic protein-like mols. of nonlinear architecture with mol. masses in the 10-20 kDa range. To synthesize such compds. of higher mol. mass and complexity, chemoselective ligation of natural (as opposed to synthetic) peptide building blocks was studied. In preliminary expts. with model peptides, conditions for the formation of peptide oximes were investigated, and their stability at alkaline pH was examined, to resolve a literature controversy. It was found that low pH (down to 2.1) was suitable for polyoxime formation and that the oxime bond was stable for up to 65 h at pH 8 and for more than 2 h at pH 9. Then, using natural peptides, it was found to be possible to synthesize, and characterize by mass spectrometry, nine-component species with mol. masses >48 kDa. This is about twice the size of homogeneous artificial proteins previously described. Such complex mols. of defined structure are beginning to find applications as vaccine candidates, as radioimmunodiagnostic agents, and as nonviral gene therapy delivery vehicles.
ST protein oxime conjugate prepn characterization; peptide oxime conjugate prepn characterization
IT Oximation
(preparation of large protein-like mols. with hydrazone and oxime linkages using natural peptide building blocks)
IT Peptides, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of large protein-like mols. with hydrazone and oxime linkages using natural peptide building blocks)

IT Hydrazones
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of large protein-like mols. with hydrazone and oxime linkages using natural peptide building blocks)

IT Oximes
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of large protein-like mols. with hydrazone and oxime linkages using natural peptide building blocks)

IT Proteins, preparation
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of large protein-like mols. with hydrazone and oxime linkages using natural peptide building blocks)

IT 3674-06-4 10329-74-5 **12584-58-6**, Porcine **insulin**
65742-92-9 71989-33-8 71989-38-3D, resin-bound 78081-87-5
153983-17-6 153983-19-8 160818-37-1 174656-50-9 **180513-42-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of large protein-like mols. with hydrazone and oxime linkages using natural peptide building blocks)

IT 141173-06-0P 160818-51-9P 180387-70-6P 180387-71-7P 180387-72-8P
180513-43-3P 180513-45-5P 180513-46-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of large protein-like mols. with hydrazone and oxime linkages using natural peptide building blocks)

IT 160966-09-6P 180387-73-9P **180686-57-1P 180686-58-2P**
180721-67-9P 180855-30-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of large protein-like mols. with hydrazone and oxime linkages using natural peptide building blocks)

=> fil reg
FILE 'REGISTRY' ENTERED AT 08:07:17 ON 25 MAY 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 23 MAY 2004 HIGHEST RN 685087-62-1
DICTIONARY FILE UPDATES: 23 MAY 2004 HIGHEST RN 685087-62-1

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> => d ide can l114

L114 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN **9004-10-8** REGISTRY
CN Insulin (9CI) (CA INDEX NAME)
OTHER NAMES:

CN Actrapid
CN Actrapid HM
CN Actrapid MC
CN Decurvon
CN Dermulin
CN Endopancrine
CN Exubera
CN HMR 4006
CN Iletin
CN Insular
CN Insulin Injection
CN Insulyl
CN Intesulin B
CN Iszilin
CN Mixtard
CN Musulin
DR 8049-67-0, 8049-95-4, 9004-12-0, 9037-76-7, 9045-63-0, 9045-65-2, 9045-66-3, 9045-67-4, 9066-39-1, 9066-40-4, 11081-38-2, 57126-42-8, 37243-75-7, 37294-43-2, 69090-47-7, 88026-11-3, 88026-12-4
MF Unspecified
CI PMS, COM, MAN
PCT Manual registration
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, CSNB, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IPA, MEDLINE, MRCK*, NAPRALERT, NIOSHTIC, PDLCOM*, PHAR, PIRA, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, VTB
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent; Report
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.P Roles for non-specific derivatives from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); MSC (Miscellaneous); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses); NORL (No role in record)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
96544 REFERENCES IN FILE CA (1907 TO DATE)
1624 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
96693 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 140:363120

REFERENCE 2: 140:363055

REFERENCE 3: 140:363053

REFERENCE 4: 140:363043

REFERENCE 5: 140:363015

REFERENCE 6: 140:362978

REFERENCE 7: 140:362838

REFERENCE 8: 140:362812

REFERENCE 9: 140:362776

REFERENCE 10: 140:362775

=> d l113 sqide nte can tot

L113 ANSWER 1 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN 290293-08-2 REGISTRY
CN (1A-21A),(1B-22B)-Insulin (human), NA-[[2-(methylsulfonyl)ethoxy]carbonyl]-
(9CI) (CA INDEX NAME)
OTHER NAMES:
CN 8: PN: WO0050456 SEQID: 1-19 claimed sequence
FS PROTEIN SEQUENCE
SQL 43,22,21
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2000050456 claimed SEQID 1-19

SEQ 1 FVNQHLCGSH LVEALYLVCG ER

SEQ 1 GIVEQCCTSI CSLYQLENYC N

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C213 H325 N56 O70 S7
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation);
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

These are the hit Sequences from ref 1-3, ref 405, pages 3-8

REFERENCE 1: 133:203411

L113 ANSWER 2 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN 290292-93-2 REGISTRY
CN (1A-21A),(1B-26B)-Insulin (human), NB,NB'-(1,8-dioxo-1,8-octanediyl)bis[26B-L-α-glutamine- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 19: PN: WO0050456 SEQID: 1-19 claimed sequence
FS PROTEIN SEQUENCE
SQL 94,26,26,21,21
NTE multichain
modified (modifications unspecified)

type	location		location	description
bridge	Phe-1	-	Phe-1'	covalent bridge
bridge	Cys-7	-	Cys-7''	disulfide bridge
bridge	Cys-19	-	Cys-20''	disulfide bridge
bridge	Cys-7'	-	Cys-7'''	disulfide bridge
bridge	Cys-19'	-	Cys-20''''	disulfide bridge
bridge	Cys-6''	-	Cys-11''	disulfide bridge
bridge	Cys-6'''	-	Cys-11''''	disulfide bridge

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2000050456 claimed SEQID 1-19

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFE
========== ========== =====
HITS AT: 1-25

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFE
========== ========== =====
HITS AT: 1-25

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21
MF C476 H708 N122 O144 S12
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain
modified (modifications unspecified)

type	location		location	description

```
bridge          Phe-1       - Phe-1'      covalent bridge
bridge          Cys-7       - Cys-7''     disulfide bridge
bridge          Cys-19      - Cys-20''    disulfide bridge
bridge          Cys-7'      - Cys-7'''    disulfide bridge
bridge          Cys-19'     - Cys-20'''   disulfide bridge
bridge          Cys-6''     - Cys-11''    disulfide bridge
bridge          Cys-6'''    - Cys-11'''   disulfide bridge
-------------------------------------------------------------------

REFERENCE   1:  133:203411

L113 ANSWER 3 OF 22  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   290292-92-1  REGISTRY
CN   (1A-21A),(1B-26B)-Insulin (human), NA-[[2-(methylsulfonyl)ethoxy]carbonyl]-
     26B-L-α-glutamine- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   18: PN: WO0050456 SEQID: 1-19 claimed sequence
FS   PROTEIN SEQUENCE
SQL  47,26,21
NTE  multichain
     modified (modifications unspecified)
-------------------------------------------------------------------
 type           ------ location ------         description
-------------------------------------------------------------------
bridge          Cys-7       - Cys-7'      disulfide bridge
bridge          Cys-19      - Cys-20'     disulfide bridge
bridge          Cys-6'      - Cys-11'     disulfide bridge
-------------------------------------------------------------------

PATENT ANNOTATIONS (PNTE):
Sequence |Patent
Source   |Reference
=========+============
Not Given|WO2000050456
         |claimed
         |SEQID 1-19


SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFE
           ========== ========== =====
HITS AT:   1-25

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF   C238 H355 N61 O75 S7
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL
DT.CA  CAplus document type:  Patent
RL.P   Roles from patents:  PREP (Preparation); RACT (Reactant or reagent)
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE  multichain
     modified (modifications unspecified)
-------------------------------------------------------------------
 type           ------ location ------         description
-------------------------------------------------------------------
bridge          Cys-7       - Cys-7'      disulfide bridge
bridge          Cys-19      - Cys-20'     disulfide bridge
bridge          Cys-6'      - Cys-11'     disulfide bridge
```

REFERENCE 1: 133:203411

L113 ANSWER 4 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN 290292-91-0 REGISTRY
CN (1A-21A),(1B-26B)-Insulin (human), NB,NB'-(1,8-dioxo-1,8-octanediyl)bis[26B-D-alaninamide- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 16: PN: WO0050456 SEQID: 1-19 claimed sequence
FS PROTEIN SEQUENCE
SQL 94,26,26,21,21
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Phe-1	- Phe-1'	covalent bridge
bridge	Cys-7	- Cys-7''	disulfide bridge
bridge	Cys-19	- Cys-20''	disulfide bridge
bridge	Cys-7'	- Cys-7'''	disulfide bridge
bridge	Cys-19'	- Cys-20'''	disulfide bridge
bridge	Cys-6''	- Cys-11''	disulfide bridge
bridge	Cys-6'''	- Cys-11'''	disulfide bridge

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2000050456 claimed SEQID 1-19

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFA
========== ========== =====
HITS AT: 1-25

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFA
========== ========== =====
HITS AT: 1-25

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21
MF C472 H704 N122 O140 S12
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain
modified (modifications unspecified)

type	------ location ------		description

bridge	Phe-1	- Phe-1'	covalent bridge
bridge	Cys-7	- Cys-7''	disulfide bridge
bridge	Cys-19	- Cys-20''	disulfide bridge
bridge	Cys-7'	- Cys-7'''	disulfide bridge
bridge	Cys-19'	- Cys-20'''	disulfide bridge
bridge	Cys-6''	- Cys-11''	disulfide bridge
bridge	Cys-6'''	- Cys-11'''	disulfide bridge

REFERENCE 1: 133:203411

L113 ANSWER 5 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN 290292-67-0 REGISTRY
CN (1A-21A),(1B-26B)-Insulin (human), NA-[[2-(methylsulfonyl)ethoxy]carbonyl]-26B-D-alaninamide- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 15: PN: WO0050456 SEQID: 1-19 claimed sequence
FS PROTEIN SEQUENCE
SQL 47,26,21
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2000050456 claimed SEQID 1-19

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFA
========== ========== =====
HITS AT: 1-25

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C236 H353 N61 O73 S7
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge

bridge Cys-6' - Cys-11' disulfide bridge

REFERENCE 1: 133:203411

L113 ANSWER 6 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN 290292-66-9 REGISTRY
CN (1A-21A),(1B-26B)-Insulin (human), NB,NB'-(1,8-dioxo-1,8-octanediyl)bis[26B-(N2-methylglycinamide)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 13: PN: WO0050456 SEQID: 1-19 claimed sequence
FS PROTEIN SEQUENCE
SQL 94,26,26,21,21
NTE multichain
modified (modifications unspecified)

type	location			description
bridge	Phe-1	-	Phe-1'	covalent bridge
bridge	Cys-7	-	Cys-7''	disulfide bridge
bridge	Cys-19	-	Cys-20''	disulfide bridge
bridge	Cys-7'	-	Cys-7'''	disulfide bridge
bridge	Cys-19'	-	Cys-20'''	disulfide bridge
bridge	Cys-6''	-	Cys-11''	disulfide bridge
bridge	Cys-6'''	-	Cys-11'''	disulfide bridge
uncommon	Sar-26		-	-
uncommon	Sar-26'		-	-

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2000050456 claimed SEQID 1-19

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFX
========== ========== =====
HITS AT: 1-25

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFX
========== ========== =====
HITS AT: 1-25

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21
MF C472 H704 N122 O140 S12
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain

modified (modifications unspecified)

type	------ location ------		description
bridge	Phe-1	- Phe-1'	covalent bridge
bridge	Cys-7	- Cys-7''	disulfide bridge
bridge	Cys-19	- Cys-20''	disulfide bridge
bridge	Cys-7'	- Cys-7'''	disulfide bridge
bridge	Cys-19'	- Cys-20'''	disulfide bridge
bridge	Cys-6''	- Cys-11''	disulfide bridge
bridge	Cys-6'''	- Cys-11'''	disulfide bridge
uncommon	Sar-26	-	-
uncommon	Sar-26'	-	-

REFERENCE 1: 133:203411

L113 ANSWER 7 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN 290292-65-8 REGISTRY
CN (1A-21A),(1B-26B)-Insulin (human), NA-[[2-(methylsulfonyl)ethoxy]carbonyl]-26B-(N2-methylglycinamide)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 11: PN: WO0050456 SEQID: 1-19 claimed sequence
FS PROTEIN SEQUENCE
SQL 47,26,21
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge
uncommon	Sar-26	-	-

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2000050456 claimed SEQID 1-19

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFX
========== ========== =====
HITS AT: 1-25

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C236 H353 N61 O73 S7
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain

modified (modifications unspecified)

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge
uncommon	Sar-26	-	-

REFERENCE 1: 133:203411

L113 ANSWER 8 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN 290292-63-6 REGISTRY
CN (1A-21A),(1B-26B)-Insulin (human), 26B-L-α-glutamine- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4: PN: WO0050456 SEQID: 1-19 claimed sequence
FS PROTEIN SEQUENCE
SQL 47,26,21
NTE multichain
modified

type	------ location ------		description
terminal mod.	Glu-26	-	C-terminal amide
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2000050456 claimed SEQID 1-19

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFE
========== ========== =====
HITS AT: 1-25

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C234 H349 N61 O71 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain
modified

type	------ location ------		description

```
-------------------------------------------------------------------------
terminal mod.    Glu-26          -          C-terminal amide
bridge           Cys-7       - Cys-7'       disulfide bridge
bridge           Cys-19      - Cys-20'      disulfide bridge
bridge           Cys-6'      - Cys-11'      disulfide bridge
-------------------------------------------------------------------------

REFERENCE   1:  133:203411

L113 ANSWER 9 OF 22  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   290292-50-1  REGISTRY
CN   (1A-21A),(1B-26B)-Insulin (human), 26B-(N2-methylglycinamide)- (9CI)  (CA
     INDEX NAME)
OTHER NAMES:
CN   2: PN: WO0050456 SEQID: 1-19 claimed sequence
CN   9: PN: WO0050456 SEQID: 1-19 claimed sequence
FS   PROTEIN SEQUENCE
SQL  47,26,21
NTE  multichain
     modified
-------------------------------------------------------------------------
 type            ------ location ------         description
-------------------------------------------------------------------------
terminal mod.    Sar-26          -          C-terminal amide
bridge           Cys-7       - Cys-7'       disulfide bridge
bridge           Cys-19      - Cys-20'      disulfide bridge
bridge           Cys-6'      - Cys-11'      disulfide bridge
uncommon         Sar-26          -          -
-------------------------------------------------------------------------

PATENT ANNOTATIONS (PNTE):
Sequence |Patent
Source   |Reference
=========+============
Not Given|WO2000050456
         |claimed
         |SEQID 1-19


SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFX
           ========== ========== =====
HITS AT:   1-25

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF   C232 H347 N61 O69 S6
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL
DT.CA  CAplus document type:  Patent
RL.P   Roles from patents:  PREP (Preparation); RACT (Reactant or reagent)
RLD.P  Roles for non-specific derivatives from patents:  BIOL (Biological
       study); PREP (Preparation); USES (Uses)
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE  multichain
     modified
-------------------------------------------------------------------------
 type            ------ location ------         description
```

terminal mod.	Sar-26	-	C-terminal amide
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge
uncommon	Sar-26	-	-

REFERENCE 1: 133:203411

L113 ANSWER 10 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN 224778-24-9 REGISTRY
CN (1A-21A),(1B-26B)-Insulin (human), 26B-D-alaninamide- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3: PN: WO0050456 SEQID: 1-19 claimed protein
FS PROTEIN SEQUENCE
SQL 47,26,21
NTE multichain

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2000050456 claimed SEQID 1-19

```
SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFA
           ========== ========== =====
HITS AT:   1-25

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21
```

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C232 H347 N61 O69 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Journal; Patent
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP Roles from non-patents: PREP (Preparation); PRP (Properties)
2 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

REFERENCE 1: 133:203411

REFERENCE 2: 130:347517

L113 ANSWER 11 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180855-30-5 REGISTRY
CN Insulin (human), 30B-L-phenylalanine-, tetraamide with N-[N2,N6-bis[N2,N6-bis[[[2-[(2-aminoethyl)amino]-2-oxoethoxy]imino]acetyl]-L-lysyl]-L-lysyl]-L-tyrosine (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 212,34,32,31,31,21,21,21,21
NTE multichain

type	------ location ------		description
bridge	Cys-7	- Cys-7[4']	disulfide bridge
bridge	Cys-19	- Cys-20[4']	disulfide bridge
bridge	Lys-32	- Oaa-31''	amide bridge
bridge	Lys-33	- Lys-32'	amide bridge
bridge	Cys-7'	- Cys-7[5']	disulfide bridge
bridge	Cys-19'	- Cys-20[5']	disulfide bridge
bridge	Lys-32'	- Oaa-31'''	amide bridge
bridge	Cys-7''	- Cys-7[6']	disulfide bridge
bridge	Cys-19''	- Cys-20[6']	disulfide bridge
bridge	Cys-7'''	- Cys-7[7']	disulfide bridge
bridge	Cys-19'''	- Cys-20[7']	disulfide bridge
bridge	Cys-6[4']	- Cys-11[4']	disulfide bridge
bridge	Cys-6[5']	- Cys-11[5']	disulfide bridge
bridge	Cys-6[6']	- Cys-11[6']	disulfide bridge
bridge	Cys-6[7']	- Cys-11[7']	disulfide bridge
uncommon	Oaa-31	-	-
uncommon	Oaa-31'	-	-
uncommon	Oaa-31''	-	-
uncommon	Oaa-31'''	-	-

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF XKKY
========== ========== =====
HITS AT: 1-25

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF XK
========== ========== =====
HITS AT: 1-25

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF X
========== ========== =====
HITS AT: 1-25

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF X
========== ========== =====
HITS AT: 1-25

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21

SEQ 1 GIVEQCCTSI CSLYQLENYC N

```
           ========== ========== =
HITS AT:   1-21

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS
DT.CA  CAplus document type:  Journal
RL.NP  Roles from non-patents:  PREP (Preparation)
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE  multichain
```

type	location		description
bridge	Cys-7	- Cys-7[4']	disulfide bridge
bridge	Cys-19	- Cys-20[4']	disulfide bridge
bridge	Lys-32	- Oaa-31''	amide bridge
bridge	Lys-33	- Lys-32'	amide bridge
bridge	Cys-7'	- Cys-7[5']	disulfide bridge
bridge	Cys-19'	- Cys-20[5']	disulfide bridge
bridge	Lys-32'	- Oaa-31'''	amide bridge
bridge	Cys-7''	- Cys-7[6']	disulfide bridge
bridge	Cys-19''	- Cys-20[6']	disulfide bridge
bridge	Cys-7'''	- Cys-7[7']	disulfide bridge
bridge	Cys-19'''	- Cys-20[7']	disulfide bridge
bridge	Cys-6[4']	- Cys-11[4']	disulfide bridge
bridge	Cys-6[5']	- Cys-11[5']	disulfide bridge
bridge	Cys-6[6']	- Cys-11[6']	disulfide bridge
bridge	Cys-6[7']	- Cys-11[7']	disulfide bridge
uncommon	Oaa-31	-	-
uncommon	Oaa-31'	-	-
uncommon	Oaa-31''	-	-
uncommon	Oaa-31'''	-	-

```
REFERENCE   1:  125:196368

L113 ANSWER 12 OF 22  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   180721-67-9  REGISTRY
CN   Insulin (swine), NB-[(aminooxy)acetyl]-, (1''''''''→1B),(1''''''''.
     fwdarw.1'B),(1'''''''''→1''B),(1'''''''''→1'''B),(1'''''''''
     '→1''''B),(1''''''''''→1'''''B),(1'''''''''''→1''''''
     B),(1'''''''''''→1'''''''B)-octaaldoxime with N2,N6-bis[N2,N6-
     bis[N2,N6-bis(oxoacetyl)-L-lysyl]-L-lysyl]-L-lysyl-L-tyrosine (9CI)  (CA
     INDEX NAME)
OTHER CA INDEX NAMES:
CN   Insulin (pig), NB-[[[(carboxymethylene)amino]oxy]acetyl]-, octaamide with
     N2,N6-bis(N2,N6-di-L-lysyl-L-lysyl)-L-lysyl-L-tyrosine
FS   PROTEIN SEQUENCE
SQL  416,30,30,30,30,30,30,30,30,21,21,21,21,21,21,21,21,4,2,1,1
NTE  multichain
```

type	location		description
bridge	Phe-1	- Lys-1[16']	covalent bridge
bridge	Cys-7	- Cys-7[8']	disulfide bridge
bridge	Cys-19	- Cys-20[8']	disulfide bridge

```
bridge          Phe-1'        - Lys-1[16']  covalent bridge
bridge          Cys-7'        - Cys-7[9']   disulfide bridge
bridge          Cys-19'       - Cys-20[9']  disulfide bridge
bridge          Phe-1''       - Lys-1[18']  covalent bridge
bridge          Cys-7''       - Cys-7[10']  disulfide bridge
bridge          Cys-19''      - Cys-20[10'] disulfide bridge
bridge          Phe-1'''      - Lys-1[18']  covalent bridge
bridge          Cys-7'''      - Cys-7[11']  disulfide bridge
bridge          Cys-19'''     - Cys-20[9']  disulfide bridge
bridge          Phe-1[4']     - Lys-1[17']  covalent bridge
bridge          Cys-7[4']     - Cys-7[12']  disulfide bridge
bridge          Cys-19[4']    - Cys-20[12'] disulfide bridge
bridge          Phe-1[5']     - Lys-1[17']  covalent bridge
bridge          Cys-7[5']     - Cys-7[13']  disulfide bridge
bridge          Cys-19[5']    - Cys-20[13'] disulfide bridge
bridge          Phe-1[6']     - Lys-1[19']  covalent bridge
bridge          Cys-7[6']     - Cys-7[14']  disulfide bridge
bridge          Cys-19[6']    - Cys-20[14'] disulfide bridge
bridge          Phe-1[7']     - Lys-1[19']  covalent bridge
bridge          Cys-7[7']     - Cys-7[15']  disulfide bridge
bridge          Cys-19[7']    - Cys-20[15'] disulfide bridge
bridge          Cys-6[8']     - Cys-11[8']  disulfide bridge
bridge          Cys-6[9']     - Cys-11[9']  disulfide bridge
bridge          Cys-6[10']    - Cys-11[10'] disulfide bridge
bridge          Cys-6[11']    - Cys-11[11'] disulfide bridge
bridge          Cys-6[12']    - Cys-11[12'] disulfide bridge
bridge          Cys-6[13']    - Cys-11[13'] disulfide bridge
bridge          Cys-6[14']    - Cys-11[14'] disulfide bridge
bridge          Cys-6[15']    - Cys-11[15'] disulfide bridge
bridge          Lys-2[16']    - Lys-1[18']  amide bridge
bridge          Lys-3[16']    - Lys-2[17']  amide bridge
bridge          Lys-2[17']    - Lys-1[19']  amide bridge
--------------------------------------------------------------------------

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKA
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKA
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKA
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKA
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKA
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKA
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKA
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKA
```

```
          ========== ========== =====
HITS AT:  1-25

SEQ     1 GIVEQCCTSI CSLYQLENYC N
          ========== ========== =
HITS AT:  1-21

SEQ     1 GIVEQCCTSI CSLYQLENYC N
          ========== ========== =
HITS AT:  1-21

SEQ     1 GIVEQCCTSI CSLYQLENYC N
          ========== ========== =
HITS AT:  1-21

SEQ     1 GIVEQCCTSI CSLYQLENYC N
          ========== ========== =
HITS AT:  1-21

SEQ     1 GIVEQCCTSI CSLYQLENYC N
          ========== ========== =
HITS AT:  1-21

SEQ     1 GIVEQCCTSI CSLYQLENYC N
          ========== ========== =
HITS AT:  1-21

SEQ     1 GIVEQCCTSI CSLYQLENYC N
          ========== ========== =
HITS AT:  1-21

SEQ     1 GIVEQCCTSI CSLYQLENYC N
          ========== ========== =
HITS AT:  1-21

SEQ     1 KKKY

SEQ     1 KK

SEQ     1 K

SEQ     1 K
MF    Unspecified
CI    MAN
SR    CA
LC    STN Files:   CA, CAPLUS
DT.CA   CAplus document type:  Journal
RL.NP   Roles from non-patents:  PREP (Preparation)
              1 REFERENCES IN FILE CA (1907 TO DATE)
              1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE   multichain
```

type	------ location ------		description
bridge	Phe-1	- Lys-1[16']	covalent bridge
bridge	Cys-7	- Cys-7[8']	disulfide bridge
bridge	Cys-19	- Cys-20[8']	disulfide bridge
bridge	Phe-1'	- Lys-1[16']	covalent bridge
bridge	Cys-7'	- Cys-7[9']	disulfide bridge
bridge	Cys-19'	- Cys-20[9']	disulfide bridge
bridge	Phe-1''	- Lys-1[18']	covalent bridge
bridge	Cys-7''	- Cys-7[10']	disulfide bridge
bridge	Cys-19''	- Cys-20[10']	disulfide bridge

bridge	Phe-1'''	- Lys-1[18']	covalent bridge
bridge	Cys-7'''	- Cys-7[11']	disulfide bridge
bridge	Cys-19'''	- Cys-20[9']	disulfide bridge
bridge	Phe-1[4']	- Lys-1[17']	covalent bridge
bridge	Cys-7[4']	- Cys-7[12']	disulfide bridge
bridge	Cys-19[4']	- Cys-20[12']	disulfide bridge
bridge	Phe-1[5']	- Lys-1[17']	covalent bridge
bridge	Cys-7[5']	- Cys-7[13']	disulfide bridge
bridge	Cys-19[5']	- Cys-20[13']	disulfide bridge
bridge	Phe-1[6']	- Lys-1[19']	covalent bridge
bridge	Cys-7[6']	- Cys-7[14']	disulfide bridge
bridge	Cys-19[6']	- Cys-20[14']	disulfide bridge
bridge	Phe-1[7']	- Lys-1[19']	covalent bridge
bridge	Cys-7[7']	- Cys-7[15']	disulfide bridge
bridge	Cys-19[7']	- Cys-20[15']	disulfide bridge
bridge	Cys-6[8']	- Cys-11[8']	disulfide bridge
bridge	Cys-6[9']	- Cys-11[9']	disulfide bridge
bridge	Cys-6[10']	- Cys-11[10']	disulfide bridge
bridge	Cys-6[11']	- Cys-11[11']	disulfide bridge
bridge	Cys-6[12']	- Cys-11[12']	disulfide bridge
bridge	Cys-6[13']	- Cys-11[13']	disulfide bridge
bridge	Cys-6[14']	- Cys-11[14']	disulfide bridge
bridge	Cys-6[15']	- Cys-11[15']	disulfide bridge
bridge	Lys-2[16']	- Lys-1[18']	amide bridge
bridge	Lys-3[16']	- Lys-2[17']	amide bridge
bridge	Lys-2[17']	- Lys-1[19']	amide bridge

REFERENCE 1: 125:196368

L113 ANSWER 13 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180686-58-2 REGISTRY
CN Insulin (human), 30B-L-phenylalanine-, 30B-[(carboxymethylene)hydrazide], octaamide with N2,N6-bis(N2,N6-di-L-lysyl-L-lysyl)-L-lysyl-L-tyrosine (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 424,35,33,32,32,31,31,31,31,21,21,21,21,21,21,21,21
NTE multichain

type	location		description
bridge	Cys-7	- Cys-7[8']	disulfide bridge
bridge	Cys-19	- Cys-20[8']	disulfide bridge
bridge	Lys-32	- Oaa-31[4']	amide bridge
bridge	Lys-33	- Lys-32''	amide bridge
bridge	Lys-34	- Lys-33'	amide bridge
bridge	Cys-7'	- Cys-7[9']	disulfide bridge
bridge	Cys-19'	- Cys-20[9']	disulfide bridge
bridge	Lys-32'	- Oaa-31[6']	amide bridge
bridge	Lys-33'	- Lys-32'''	amide bridge
bridge	Cys-7''	- Cys-7[10']	disulfide bridge
bridge	Cys-19''	- Cys-20[10']	disulfide bridge
bridge	Lys-32''	- Oaa-31[5']	amide bridge
bridge	Cys-7'''	- Cys-7[11']	disulfide bridge
bridge	Cys-19'''	- Cys-20[9']	disulfide bridge
bridge	Lys-32'''	- Oaa-31[7']	amide bridge
bridge	Cys-7[4']	- Cys-7[12']	disulfide bridge
bridge	Cys-19[4']	- Cys-20[12']	disulfide bridge
bridge	Cys-7[5']	- Cys-7[13']	disulfide bridge
bridge	Cys-19[5']	- Cys-20[13']	disulfide bridge
bridge	Cys-7[6']	- Cys-7[14']	disulfide bridge
bridge	Cys-19[6']	- Cys-20[14']	disulfide bridge
bridge	Cys-7[7']	- Cys-7[15']	disulfide bridge

```
bridge          Cys-19[7']   - Cys-20[15'] disulfide bridge
bridge          Cys-6[8']    - Cys-11[8']  disulfide bridge
bridge          Cys-6[9']    - Cys-11[9']  disulfide bridge
bridge          Cys-6[10']   - Cys-11[10'] disulfide bridge
bridge          Cys-6[11']   - Cys-11[11'] disulfide bridge
bridge          Cys-6[12']   - Cys-11[12'] disulfide bridge
bridge          Cys-6[13']   - Cys-11[13'] disulfide bridge
bridge          Cys-6[14']   - Cys-11[14'] disulfide bridge
bridge          Cys-6[15']   - Cys-11[15'] disulfide bridge
uncommon        Oaa-31         -          -
uncommon        Oaa-31'        -          -
uncommon        Oaa-31''       -          -
uncommon        Oaa-31'''      -          -
uncommon        Oaa-31[4']     -          -
uncommon        Oaa-31[5']     -          -
uncommon        Oaa-31[6']     -          -
uncommon        Oaa-31[7']     -          -
-------------------------------------------------------------------------

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF XKKKY
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF XKK
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF XK
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF XK
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF X
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF X
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF X
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF X
           ========== ========== =====
HITS AT:   1-25

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21
```

```
SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS
DT.CA  CAplus document type:  Journal
RL.NP  Roles from non-patents:  PREP (Preparation)
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE  multichain
```

type	------ location ------			description
bridge	Cys-7	-	Cys-7[8']	disulfide bridge
bridge	Cys-19	-	Cys-20[8']	disulfide bridge
bridge	Lys-32	-	Oaa-31[4']	amide bridge
bridge	Lys-33	-	Lys-32''	amide bridge
bridge	Lys-34	-	Lys-33'	amide bridge
bridge	Cys-7'	-	Cys-7[9']	disulfide bridge
bridge	Cys-19'	-	Cys-20[9']	disulfide bridge
bridge	Lys-32'	-	Oaa-31[6']	amide bridge
bridge	Lys-33'	-	Lys-32'''	amide bridge
bridge	Cys-7''	-	Cys-7[10']	disulfide bridge
bridge	Cys-19''	-	Cys-20[10']	disulfide bridge
bridge	Lys-32''	-	Oaa-31[5']	amide bridge
bridge	Cys-7'''	-	Cys-7[11']	disulfide bridge
bridge	Cys-19'''	-	Cys-20[9']	disulfide bridge
bridge	Lys-32'''	-	Oaa-31[7']	amide bridge
bridge	Cys-7[4']	-	Cys-7[12']	disulfide bridge
bridge	Cys-19[4']	-	Cys-20[12']	disulfide bridge
bridge	Cys-7[5']	-	Cys-7[13']	disulfide bridge
bridge	Cys-19[5']	-	Cys-20[13']	disulfide bridge
bridge	Cys-7[6']	-	Cys-7[14']	disulfide bridge
bridge	Cys-19[6']	-	Cys-20[14']	disulfide bridge
bridge	Cys-7[7']	-	Cys-7[15']	disulfide bridge
bridge	Cys-19[7']	-	Cys-20[15']	disulfide bridge
bridge	Cys-6[8']	-	Cys-11[8']	disulfide bridge
bridge	Cys-6[9']	-	Cys-11[9']	disulfide bridge
bridge	Cys-6[10']	-	Cys-11[10']	disulfide bridge
bridge	Cys-6[11']	-	Cys-11[11']	disulfide bridge
bridge	Cys-6[12']	-	Cys-11[12']	disulfide bridge
bridge	Cys-6[13']	-	Cys-11[13']	disulfide bridge
bridge	Cys-6[14']	-	Cys-11[14']	disulfide bridge
bridge	Cys-6[15']	-	Cys-11[15']	disulfide bridge
uncommon	Oaa-31	-	-	

uncommon	Oaa-31'	-	-
uncommon	Oaa-31''	-	-
uncommon	Oaa-31'''	-	-
uncommon	Oaa-31[4']	-	-
uncommon	Oaa-31[5']	-	-
uncommon	Oaa-31[6']	-	-
uncommon	Oaa-31[7']	-	-

REFERENCE 1: 125:196368

L113 ANSWER 14 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN **180686-57-1** REGISTRY
CN Insulin (human), 30B-L-phenylalanine-, 30B-[(carboxymethylene)hydrazide], tetraamide with N2,N6-di-L-lysyl-L-lysyl-L-tyrosine (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE
SQL 212,34,32,31,31,21,21,21,21
NTE multichain

type	location		description
bridge	Cys-7	- Cys-7[4']	disulfide bridge
bridge	Cys-19	- Cys-20[4']	disulfide bridge
bridge	Lys-32	- Oaa-31''	amide bridge
bridge	Lys-33	- Lys-32'	amide bridge
bridge	Cys-7'	- Cys-7[5']	disulfide bridge
bridge	Cys-19'	- Cys-20[5']	disulfide bridge
bridge	Lys-32'	- Oaa-31'''	amide bridge
bridge	Cys-7''	- Cys-7[6']	disulfide bridge
bridge	Cys-19''	- Cys-20[6']	disulfide bridge
bridge	Cys-7'''	- Cys-7[7']	disulfide bridge
bridge	Cys-19'''	- Cys-20[7']	disulfide bridge
bridge	Cys-6[4']	- Cys-11[4']	disulfide bridge
bridge	Cys-6[5']	- Cys-11[5']	disulfide bridge
bridge	Cys-6[6']	- Cys-11[6']	disulfide bridge
bridge	Cys-6[7']	- Cys-11[7']	disulfide bridge
uncommon	Oaa-31	-	-
uncommon	Oaa-31'	-	-
uncommon	Oaa-31''	-	-
uncommon	Oaa-31'''	-	-

```
SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF XKKY
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF XK
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF X
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF X
           ========== ========== =====
HITS AT:   1-25

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

SEQ      1 GIVEQCCTSI CSLYQLENYC N
```

```
          ========== ========== =
HITS AT:  1-21

SEQ       1 GIVEQCCTSI CSLYQLENYC N
          ========== ========== =
HITS AT:  1-21

SEQ       1 GIVEQCCTSI CSLYQLENYC N
          ========== ========== =
HITS AT:  1-21

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF   Unspecified
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS
DT.CA  CAplus document type:  Journal
RL.NP  Roles from non-patents:  PREP (Preparation)
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE  multichain
```

type	------ location ------		description
bridge	Cys-7	- Cys-7[4']	disulfide bridge
bridge	Cys-19	- Cys-20[4']	disulfide bridge
bridge	Lys-32	- Oaa-31''	amide bridge
bridge	Lys-33	- Lys-32'	amide bridge
bridge	Cys-7'	- Cys-7[5']	disulfide bridge
bridge	Cys-19'	- Cys-20[5']	disulfide bridge
bridge	Lys-32'	- Oaa-31'''	amide bridge
bridge	Cys-7''	- Cys-7[6']	disulfide bridge
bridge	Cys-19''	- Cys-20[6']	disulfide bridge
bridge	Cys-7'''	- Cys-7[7']	disulfide bridge
bridge	Cys-19'''	- Cys-20[7']	disulfide bridge
bridge	Cys-6[4']	- Cys-11[4']	disulfide bridge
bridge	Cys-6[5']	- Cys-11[5']	disulfide bridge
bridge	Cys-6[6']	- Cys-11[6']	disulfide bridge
bridge	Cys-6[7']	- Cys-11[7']	disulfide bridge
uncommon	Oaa-31	-	-
uncommon	Oaa-31'	-	-
uncommon	Oaa-31''	-	-
uncommon	Oaa-31'''	-	-

```
REFERENCE   1:  125:196368

L113 ANSWER 15 OF 22  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   180513-46-6  REGISTRY
CN   Insulin (human), 30B-[N-[2-[[(aminooxy)acetyl]amino]ethyl]-L-
     phenylalaninamide]- (9CI)  (CA INDEX NAME)
FS   PROTEIN SEQUENCE
SQL  51,30,21
NTE  multichain
     modified (modifications unspecified)
```

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

```
SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKF
           ========== ========== =====
HITS AT:   1-25

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF   C266 H394 N68 O77 S6
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS
DT.CA  CAplus document type:  Journal
RL.NP  Roles from non-patents:  PREP (Preparation); RACT (Reactant or reagent)
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE  multichain
     modified (modifications unspecified)
-------------------------------------------------------------------
 type            ------ location ------         description
-------------------------------------------------------------------
bridge           Cys-7       - Cys-7'      disulfide bridge
bridge           Cys-19      - Cys-20'     disulfide bridge
bridge           Cys-6'      - Cys-11'     disulfide bridge
-------------------------------------------------------------------

REFERENCE   1:  125:196368

L113 ANSWER 16 OF 22  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   180513-45-5  REGISTRY
CN   Insulin (swine), NB-[[[[(1,1-dimethylethoxy)carbonyl]amino]oxy]acetyl]-
     (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   Insulin (pig), NB-[[[[(1,1-dimethylethoxy)carbonyl]amino]oxy]acetyl]-
FS   PROTEIN SEQUENCE
SQL  51,30,21
NTE  multichain
     modified (modifications unspecified)
-------------------------------------------------------------------
 type            ------ location ------         description
-------------------------------------------------------------------
bridge           Cys-7       - Cys-7'      disulfide bridge
bridge           Cys-19      - Cys-20'     disulfide bridge
bridge           Cys-6'      - Cys-11'     disulfide bridge
-------------------------------------------------------------------

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKA
           ========== ========== =====
HITS AT:   1-25

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
MF   C263 H392 N66 O80 S6
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS
DT.CA  CAplus document type:  Journal
RL.NP  Roles from non-patents:  PREP (Preparation); RACT (Reactant or reagent)
               1 REFERENCES IN FILE CA (1907 TO DATE)
```

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

REFERENCE 1: 125:196368

L113 ANSWER 17 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180513-43-3 REGISTRY
CN Insulin (swine), NB-[(aminooxy)acetyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Insulin (pig), NB-[(aminooxy)acetyl]-
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKA
========== ========== =====
HITS AT: 1-25

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C258 H384 N66 O78 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain
modified (modifications unspecified)

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

REFERENCE 1: 125:196368

L113 ANSWER 18 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN 180513-42-2 REGISTRY
CN (1A-21A),(1B-29B)-Insulin (human), 29B-hydrazide (9CI) (CA INDEX NAME)
FS PROTEIN SEQUENCE

SQL 50,29,21
NTE multichain
modified (modifications unspecified)

type	location		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPK
========== ========== =====
HITS AT: 1-25

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C253 H378 N66 O74 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS
DT.CA CAplus document type: Journal
RL.NP Roles from non-patents: RACT (Reactant or reagent)
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain
modified (modifications unspecified)

type	location		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

REFERENCE 1: 125:196368

L113 ANSWER 19 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN **65742-92-9** REGISTRY
CN Insulin (swine), NA-[[2-(methylsulfonyl)ethoxy]carbonyl]-29B-[N6-[[2-(methylsulfonyl)ethoxy]carbonyl]-L-lysine]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3,4,44,45,90,91-Hexathia-8,11,14,17,20,23,26,29,32,35,38,41,48,51,54,57,60,63,66,69,72,75,78,81,84,86-hexacosaazabicyclo[72.11.7]dononacontane, cyclic peptide deriv.
CN Insulin (ox), NA-[[2-(methylsulfonyl)ethoxy]carbonyl]-8A-L-threonine-10A-L-isoleucine-29B-[N6-[[2-(methylsulfonyl)ethoxy]carbonyl]-L-lysine]-
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain
modified (modifications unspecified)

type	location		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKA

```
           ========== ========== =====
HITS AT:   1-25

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
DR   66524-20-7, 76632-71-8, 148046-60-0, 88264-78-2
MF   C264 H393 N65 O84 S8
CI   MAN
LC   STN Files:   CA, CAPLUS
DT.CA  CAplus document type:  Conference; Journal; Patent
RL.P   Roles from patents:  BIOL (Biological study); RACT (Reactant or reagent)
RL.NP  Roles from non-patents:  PREP (Preparation); RACT (Reactant or reagent)
              14 REFERENCES IN FILE CA (1907 TO DATE)
              14 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE  multichain
     modified (modifications unspecified)
-------------------------------------------------------------------------
 type            ------ location ------          description
-------------------------------------------------------------------------
bridge           Cys-7       - Cys-7'      disulfide bridge
bridge           Cys-19      - Cys-20'     disulfide bridge
bridge           Cys-6'      - Cys-11'     disulfide bridge
-------------------------------------------------------------------------

REFERENCE   1:  125:196368

REFERENCE   2:  122:240399

REFERENCE   3:  119:49869

REFERENCE   4:  117:1060

REFERENCE   5:  107:109791

REFERENCE   6:  105:35762

REFERENCE   7:  104:110140

REFERENCE   8:  100:22995

REFERENCE   9:  98:215966

REFERENCE  10:  95:151147

L113 ANSWER 20 OF 22  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   39416-70-1  REGISTRY
CN   (1A-21A),(1B-22B)-Insulin (human) (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   3,4,44,45,90,91-Hexathia-8,11,14,17,20,23,26,29,32,35,38,41,48,51,54,57,60
     ,63,66,69,72,75,78,81,84,86-hexacosaazabicyclo[72.11.7]dononacontane,
     cyclic peptide deriv.
CN   Insulin (ox), 8A-L-threonine-10A-L-isoleucine-23B-deglycine-24B-de-L-
     phenylalanine-25B-de-L-phenylalanine-26B-de-L-tyrosine-27B-de-L-threonine-
     28B-de-L-proline-29B-de-L-lysine-30B-de-L-alanine-
OTHER NAMES:
CN   7: PN: WO0050456 SEQID: 1-19 claimed sequence
CN   Des(B23-30) insulin (human)
CN   Desoctapeptide insulin (porcine)
CN   Desoctapeptide-(B23-30)-insulin (pig)
FS   PROTEIN SEQUENCE
```

SQL 43,22,21
NTE multichain

type	location		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2000050456
	claimed
	SEQID 1-19

SEQ 1 FVNQHLCGSH LVEALYLVCG ER

SEQ 1 GIVEQCCTSI CSLYQLENYC N

RELATED SEQUENCES AVAILABLE WITH SEQLINK
DR 131571-12-5, 133107-16-1, 102283-03-4, 79104-11-3, 39471-21-1, 275822-90-7, 290292-64-7
MF C209 H320 N56 O66 S6
CI MAN
LC STN Files: BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, EMBASE, MEDLINE, TOXCENTER, USPATFULL
DT.CA CAplus document type: Conference; Journal; Patent
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PRP (Properties)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
86 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
86 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain

type	location		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

REFERENCE 1: 140:281562

REFERENCE 2: 140:144769

REFERENCE 3: 140:77379

REFERENCE 4: 136:891

REFERENCE 5: 133:203411

REFERENCE 6: 133:43782

REFERENCE 7: 132:343612

REFERENCE 8: 132:343611

REFERENCE 9: 128:149680

REFERENCE 10: 126:248473

L113 ANSWER 21 OF 22 REGISTRY COPYRIGHT 2004 ACS on STN
RN 12584-58-6 REGISTRY
CN Insulin (swine) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3,4,44,45,90,91-Hexathia-8,11,14,17,20,23,26,29,32,35,38,41,48,51,54,57,60,63,66,69,72,75,78,81,84,86-hexacosaazabicyclo[72.11.7]dononacontane, cyclic peptide deriv.
CN Insulin (ox), 8A-L-threonine-10A-L-isoleucine-
OTHER NAMES:
CN 2: PN: WO2004005342 PAGE: 46 claimed protein
CN Hog insulin
CN Insulin (Alopex lagopus)
CN Insulin (Canis familiaris)
CN Insulin (Physeter catodon)
CN Insulin (pig)
CN Insulin (porcine)
CN Insulin (swine)
CN L-Alanine, L-phenylalanyl-L-valyl-L-asparaginyl-L-glutaminyl-L-histidyl-L-leucyl-L-cysteinylglycyl-L-seryl-L-histidyl-L-leucyl-L-valyl-L-α-glutamyl-L-alanyl-L-leucyl-L-tyrosyl-L-leucyl-L-valyl-L-cysteinylglycyl-L-α-glutamyl-L-arginylglycyl-L-phenylalanyl-L-phenylalanyl-L-tyrosyl-L-threonyl-L-prolyl-L-lysyl-, cyclic (7→7'),(19→20')-bis(disulfide) with glycyl-L-isoleucyl-L-valyl-L-α-glutamyl-L-glutaminyl-L-cysteinyl-L-cysteinyl-L-threonyl-L-seryl-L-isoleucyl-L-cysteinyl-L-seryl-L-leucyl-L-tyrosyl-L-glutaminyl-L-leucyl-L-α-glutamyl-L-asparaginyl-L-tyrosyl-L-cysteinyl-L-asparagine cyclic (6'→11')-disulfide
CN Neutral Insulin
CN Pensulin SR
CN Pig insulin
CN Porcine insulin
CN Swine insulin
CN Velosulin
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2004005342 claimed PAGE 46

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKA
========== ========== =====
HITS AT: 1-25

```
SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

**RELATED SEQUENCES AVAILABLE WITH SEQLINK**
DR   9004-14-2, 97380-49-9, 184890-24-2
MF   C256 H381 N65 O76 S6
CI   COM, MAN
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
       CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN,
       CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA,
       MEDLINE, MRCK*, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
         (*File contains numerically searchable property data)
     Other Sources:  EINECS**
         (**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA  CAplus document type:  Book; Conference; Dissertation; Journal; Patent
RL.P   Roles from patents:  ANST (Analytical study); BIOL (Biological study);
       PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
       reagent); USES (Uses)
RLD.P  Roles for non-specific derivatives from patents:  ANST (Analytical
       study); BIOL (Biological study); PREP (Preparation); USES (Uses)
RL.NP  Roles from non-patents:  ANST (Analytical study); BIOL (Biological
       study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP
       (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
       reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents:  ANST (Analytical
       study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP
       (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
       reagent); USES (Uses)
            446 REFERENCES IN FILE CA (1907 TO DATE)
             44 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            447 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE  multichain
```

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

```
REFERENCE   1:  140:332637

REFERENCE   2:  140:281562

REFERENCE   3:  140:133626

REFERENCE   4:  140:122805

REFERENCE   5:  140:105831

REFERENCE   6:  140:77379

REFERENCE   7:  140:23397

REFERENCE   8:  139:302151

REFERENCE   9:  139:271284

REFERENCE  10:  139:240519

L113 ANSWER 22 OF 22  REGISTRY  COPYRIGHT 2004 ACS on STN
```

RN 11061-68-0 REGISTRY
CN Insulin (human) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 3,4,44,45,90,91-Hexathia-8,11,14,17,20,23,26,29,32,35,38,41,48,51,54,57,60,63,66,69,72,75,78,81,84,86-hexacosaazabicyclo[72.11.7]dononacontane, cyclic peptide deriv.
CN Insulin (ox), 8A-L-threonine-10A-L-isoleucine-30B-L-threonine-
OTHER NAMES:
CN 6: PN: WO0050456 SEQID: 1-19 claimed protein
CN H-Tronin
CN Human Insulatard
CN Human insulin
CN Human Protaphane
CN Humulin
CN Humulin N
CN Humulin N-U 100
CN Humulin R
CN Humulin S
CN Insulin (Cercopithecus aethiops)
CN Insulin (Macaca fascicularis)
CN Insulin (Macaca mulatta)
CN Insulin (Pan troglodytes)
CN Isuhuman
CN L-Threonine, L-phenylalanyl-L-valyl-L-asparaginyl-L-glutaminyl-L-histidyl-L-leucyl-L-cysteinylglycyl-L-seryl-L-histidyl-L-leucyl-L-valyl-L-α-glutamyl-L-alanyl-L-leucyl-L-tyrosyl-L-leucyl-L-valyl-L-cysteinylglycyl-L-α-glutamyl-L-arginylglycyl-L-phenylalanyl-L-phenylalanyl-L-tyrosyl-L-threonyl-L-prolyl-L-lysyl-, cyclic (7→7'),(19→20')-bis(disulfide) with glycyl-L-isoleucyl-L-valyl-L-α-glutamyl-L-glutaminyl-L-cysteinyl-L-cysteinyl-L-threonyl-L-seryl-L-isoleucyl-L-cysteinyl-L-seryl-L-leucyl-L-tyrosyl-L-glutaminyl-L-leucyl-L-α-glutamyl-L-asparaginyl-L-tyrosyl-L-cysteinyl-L-asparagine cyclic (6'→11')-disulfide
CN Novolin
CN Novolin R
CN Penfil R
CN Ultraphane
CN Velosuline HM
FS PROTEIN SEQUENCE
SQL 51,30,21
NTE multichain

type	------ location ------		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2000050456 claimed SEQID 1-19

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFYTPKT
========== ========== =====
HITS AT: 1-25

SEQ 1 GIVEQCCTSI CSLYQLENYC N

========== ========== =
HITS AT: 1-21

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C257 H383 N65 O77 S6
CI COM, MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IMSCOSEARCH, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, PROMT, RTECS*, TOXCENTER, USAN, USPAT2, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)
DT.CA CAplus document type: Book; Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP (Preparation); PROC (Process); PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RLD.NP Roles for non-specific derivatives from non-patents: ANST (Analytical study); BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)
612 REFERENCES IN FILE CA (1907 TO DATE)
90 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
614 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain

type	location		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge

REFERENCE 1: 140:350772

REFERENCE 2: 140:293377

REFERENCE 3: 140:281562

REFERENCE 4: 140:193075

REFERENCE 5: 140:157738

REFERENCE 6: 140:123005

REFERENCE 7: 140:23454

REFERENCE 8: 140:1010

REFERENCE 9: 140:1008

REFERENCE 10: 139:359064

=> => d his

```
     (FILE 'HOME' ENTERED AT 07:06:45 ON 25 MAY 2004)
               SET COST OFF

     FILE 'HCAPLUS' ENTERED AT 07:06:55 ON 25 MAY 2004
L1             1 S US20020160938/PN OR (WO2000-EP1530 OR DE99-19908041)/AP,PRN
               E HOECKER H/AU
               E BRANDENBURG D/AU
L2           277 S E3-E5,E7-E10
               E HAVENITH C/AU
L3             9 S E3-E4,E6
               E AVENTI/PA,CS
L4          2089 S E4-E6 OR AVENTIS?/PA,CS

     FILE 'REGISTRY' ENTERED AT 07:09:52 ON 25 MAY 2004
L5             1 S 9004-10-8
L6             1 S 11061-68-0
L7          7097 S INSULIN
L8          7095 S L7 NOT L5,L6

     FILE 'HCAPLUS' ENTERED AT 07:10:06 ON 25 MAY 2004
L9         97354 S L5 OR L6
L10        34776 S L8
L11       164855 S ?INSULIN?
L12            1 S L1 AND L9-L11
L13          359 S L2-L4 AND L9-L11
L14           30 S L13 AND ?DIMER?
L15            4 S L14 AND ?BRIDG?
L16           14 S L14 AND ?COVALEN?
L17           13 S L14 AND (?CROSSLINK? OR ?CROSS LINK?)
L18           20 S L15-L17
L19           10 S L14 NOT L18
L20            4 S L14 AND DES
L21            4 S L14 AND (B27 OR B30 OR B26)
L22            5 S L20,L21
L23            5 S L22 AND L15-L19
L24            6 S L12,L23
L25           24 S L14-L19 NOT L24
               SEL RN L12

     FILE 'REGISTRY' ENTERED AT 07:17:29 ON 25 MAY 2004
L26           18 S E1-E18
L27            2 S L26 AND L5,L6
L28           11 S L26 AND L8
L29            5 S L26 NOT L27,L28
L30            3 S L28 AND S>=12
L31            8 S L28 NOT L30
L32         1905 S GIVEQCCTSICSLYQLENYCN/SQSP
L33         2325 S FVNQHLCGSHLVEALYLVCGERGFF/SQSP
L34         1300 S L32 AND L33
L35          920 S L34 AND MULTICHAIN/NTE
L36          912 S L35 AND DISULFIDE BRIDGE/NTE
L37            3 S L35 AND SULFIDE BRIDGE/NTE
L38           24 S L35 AND COVALENT BRIDGE/NTE
L39           67 S L35 AND AMIDE BRIDGE/NTE
L40          920 S L36-L39
L41           10 S L26 AND L34
L42            2 S L28 NOT L41
L43            1 S L42 NOT 39416-70-1
L44           11 S L41,L43

     FILE 'HCAPLUS' ENTERED AT 07:25:30 ON 25 MAY 2004

     FILE 'REGISTRY' ENTERED AT 07:25:39 ON 25 MAY 2004
```

```
L45          10 S L44 NOT L27

     FILE 'HCAPLUS' ENTERED AT 07:25:57 ON 25 MAY 2004
L46           2 S L45
L47        1461 S L40

     FILE 'REGISTRY' ENTERED AT 07:26:19 ON 25 MAY 2004
L48         919 S L47 NOT L5,L6

     FILE 'HCAPLUS' ENTERED AT 07:26:32 ON 25 MAY 2004
L49        1108 S L48

     FILE 'REGISTRY' ENTERED AT 07:26:42 ON 25 MAY 2004
L50          12 S L48 AND S>=12

     FILE 'HCAPLUS' ENTERED AT 07:27:47 ON 25 MAY 2004
L51           5 S L50
L52           6 S L46,L51
L53           2 S L52 AND L1-L4,L12-L25

     FILE 'REGISTRY' ENTERED AT 07:28:47 ON 25 MAY 2004
L54           1 S 170712-62-6

     FILE 'HCAPLUS' ENTERED AT 07:28:54 ON 25 MAY 2004
L55           4 S L52 NOT L53
L56           4 S L55 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 07:31:41 ON 25 MAY 2004
L57           9 S E19-E27
L58           4 S L57 AND (C290H445N67O80S12 OR C264H397N67O97S12 OR C265H400N6
L59         900 S L40 AND CYS 7/NTE
L60         848 S L59 AND CYS 19/NTE
L61         806 S L60 AND CYS 6/NTE
L62          11 S L61 AND PHE 1/NTE
L63           3 S L61 AND SAR 26/NTE
L64          13 S L62,L63
L65          12 S L64 NOT FE/ELS
L66           7 S L65 NOT L45
L67           3 S L66 NOT TERMINAL MOD/NTE
L68           3 S L66 NOT TERMINAL MOD/NTE

     FILE 'HCAPLUS' ENTERED AT 07:42:24 ON 25 MAY 2004
L69           2 S L68
L70           4 S L46,L69
L71           4 S L70 AND L1-L4,L9-L25
L72         811 S L49 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)
L73          41 S L72 AND ?DIMER?
L74          29 S L72 AND ?COVALEN?
L75          13 S L72 AND ?BRIDG?
L76          35 S L72 AND (?DISULFID? OR ?DISULPHID?)
L77          96 S L73-L76
L78          95 S L77 AND L9,L11
L79          18 S L78 AND P/DT
L80           2 S L79 AND (SARB26 OR SAR B26 OR B27 OR B30 OR B26 OR SARCOSIN?)
L81           1 S L78 AND DES B27
L82           1 S L80 AND L81
L83           5 S L71,L82
L84           4 S L83 NOT L1
                SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 07:49:31 ON 25 MAY 2004
L85          41 S E28-E68
```

```
L86             3 S L85 AND L68
                  SEL RN 1
L87             2 S L86 NOT E69
L88             1 S L85 AND L45
L89             3 S L87,L88
L90            38 S L85 NOT L89
L91            10 S L90 AND 30B
L92             2 S L90 AND 26B
L93             1 S L92 NOT 25B
                  SEL RN L91 4 5
L94             2 S E70-E71
L95             6 S L93,L94,L89
L96             3 S L95 NOT 29B
L97             3 S L95 NOT L96
L98             2 S L96 NOT 117924-56-8
                  SEL RN L97 3
L99             1 S E72
L100            2 S L98,L88

     FILE 'HCAPLUS' ENTERED AT 08:01:05 ON 25 MAY 2004
L101            3 S L100
L102            3 S L46,L101
L103           29 S L14-L25 NOT L102
L104           28 S L103 AND (PY<=1999 OR PRY<=1999 OR AY<=1999)

     FILE 'HCAPLUS' ENTERED AT 08:03:12 ON 25 MAY 2004
L105            3 S L102 AND L1-L4,L9-L25,L46,L47,L49,L51-L53,L55-L56,L69-L84,L10
                  SEL HIT RN

     FILE 'REGISTRY' ENTERED AT 08:05:17 ON 25 MAY 2004
L106           23 S E73-E95
L107           21 S L106 AND L5,L6,L34
L108            2 S L106 NOT L107
L109           23 S L106,L107

     FILE 'HCAPLUS' ENTERED AT 08:07:09 ON 25 MAY 2004

     FILE 'REGISTRY' ENTERED AT 08:07:17 ON 25 MAY 2004
L110           20 S L109 AND L34
L111            3 S L109 NOT L110
L112            2 S L111 NOT L5
L113           22 S L110,L112
L114            1 S L109 NOT L113
L115            3 S L34 AND SAR 26/NTE
L116            0 S L115 NOT L109

=> d l115 sqide nte can tot

L115 ANSWER 1 OF 3  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   290292-66-9  REGISTRY
CN   (1A-21A),(1B-26B)-Insulin (human), NB,NB'-(1,8-dioxo-1,8-
     octanediyl)bis[26B-(N2-methylglycinamide)- (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   13: PN: WO0050456 SEQID: 1-19 claimed sequence
FS   PROTEIN SEQUENCE
SQL  94,26,26,21,21
NTE  multichain
     modified (modifications unspecified)
-------------------------------------------------------------------
 type            ------ location ------         description
-------------------------------------------------------------------
bridge           Phe-1       - Phe-1'      covalent bridge
bridge           Cys-7       - Cys-7''     disulfide bridge
```

```
bridge          Cys-19      - Cys-20''    disulfide bridge
bridge          Cys-7'      - Cys-7'''    disulfide bridge
bridge          Cys-19'     - Cys-20'''   disulfide bridge
bridge          Cys-6''     - Cys-11''    disulfide bridge
bridge          Cys-6'''    - Cys-11'''   disulfide bridge
uncommon        Sar-26        -           -
uncommon        Sar-26'       -           -
-----------------------------------------------------------------------

PATENT ANNOTATIONS (PNTE):
Sequence |Patent
Source   |Reference
=========+============
Not Given|WO2000050456
         |claimed
         |SEQID 1-19


SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFX
           ========== ========== =====
HITS AT:   1-25

SEQ      1 FVNQHLCGSH LVEALYLVCG ERGFFX
           ========== ========== =====
HITS AT:   1-25

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21

SEQ      1 GIVEQCCTSI CSLYQLENYC N
           ========== ========== =
HITS AT:   1-21
MF   C472 H704 N122 O140 S12
CI   MAN
SR   CA
LC   STN Files:   CA, CAPLUS, USPATFULL
DT.CA  CAplus document type:  Patent
RL.P   Roles from patents:  BIOL (Biological study); PREP (Preparation); USES
       (Uses)
              1 REFERENCES IN FILE CA (1907 TO DATE)
              1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE  multichain
     modified (modifications unspecified)
-----------------------------------------------------------------------
 type           ------ location ------        description
-----------------------------------------------------------------------
bridge          Phe-1       - Phe-1'      covalent bridge
bridge          Cys-7       - Cys-7''     disulfide bridge
bridge          Cys-19      - Cys-20''    disulfide bridge
bridge          Cys-7'      - Cys-7'''    disulfide bridge
bridge          Cys-19'     - Cys-20'''   disulfide bridge
bridge          Cys-6''     - Cys-11''    disulfide bridge
bridge          Cys-6'''    - Cys-11'''   disulfide bridge
uncommon        Sar-26        -           -
uncommon        Sar-26'       -           -
-----------------------------------------------------------------------

REFERENCE   1:  133:203411

L115 ANSWER 2 OF 3  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   290292-65-8  REGISTRY
CN   (1A-21A),(1B-26B)-Insulin (human), NA-[[2-(methylsulfonyl)ethoxy]carbonyl]-
```

26B-(N2-methylglycinamide)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 11: PN: WO0050456 SEQID: 1-19 claimed sequence
FS PROTEIN SEQUENCE
SQL 47,26,21
NTE multichain
modified (modifications unspecified)

type	location		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge
uncommon	Sar-26	-	-

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2000050456 claimed SEQID 1-19

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFX
========== ========== =====
HITS AT: 1-25

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C236 H353 N61 O73 S7
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain
modified (modifications unspecified)

type	location		description
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge
uncommon	Sar-26	-	-

REFERENCE 1: 133:203411

L115 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2004 ACS on STN
RN 290292-50-1 REGISTRY
CN (1A-21A),(1B-26B)-Insulin (human), 26B-(N2-methylglycinamide)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2: PN: WO0050456 SEQID: 1-19 claimed sequence
CN 9: PN: WO0050456 SEQID: 1-19 claimed sequence
FS PROTEIN SEQUENCE

SQL 47,26,21
NTE multichain
modified

type	location		description
terminal mod.	Sar-26	-	C-terminal amide
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge
uncommon	Sar-26	-	-

PATENT ANNOTATIONS (PNTE):

Sequence Source	Patent Reference
Not Given	WO2000050456
	claimed
	SEQID 1-19

SEQ 1 FVNQHLCGSH LVEALYLVCG ERGFFX
========== ========== =====
HITS AT: 1-25

SEQ 1 GIVEQCCTSI CSLYQLENYC N
========== ========== =
HITS AT: 1-21

RELATED SEQUENCES AVAILABLE WITH SEQLINK
MF C232 H347 N61 O69 S6
CI MAN
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
DT.CA CAplus document type: Patent
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)
RLD.P Roles for non-specific derivatives from patents: BIOL (Biological study); PREP (Preparation); USES (Uses)
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
NTE multichain
modified

type	location		description
terminal mod.	Sar-26	-	C-terminal amide
bridge	Cys-7	- Cys-7'	disulfide bridge
bridge	Cys-19	- Cys-20'	disulfide bridge
bridge	Cys-6'	- Cys-11'	disulfide bridge
uncommon	Sar-26	-	-

REFERENCE 1: 133:203411

=>